

Congress and the Prospects for Higher Education

It will be a tragedy for higher education in the United States if Congress fails to deal in an enlightened way with the Higher Education Bill (see page 365). For several years, a great many educational institutions in the United States have been driven to penury and even out of existence by the difficulty of keeping in the black. Their problems arise from the simple laws of supply and demand. Under present arrangements, most colleges and universities have to finance their teaching operations from fees collected from students. With inflation as it is, there is no escape from continuing and steep increases of tuition fees, and in the past few years it has become apparent that the student market is by no means inelastic. Many young people are being forced to recognize that tertiary education is beyond their means. The question which Congress has now to decide is not merely that of how best to devise a mechanism for channelling money to the colleges and universities but whether it wishes to see the scale of higher education in the United States determined by the necessarily arbitrary balance which is struck at any time between the level of tuition fees and the capacity of young people and their families to pay them. In a rational world, the Administration would no doubt have put forward proposals for channelling funds to institutions in higher education which are at once less arbitrary than those which Congress is now considering and less obviously designed to satisfy identifiable vested interests, but the great irony of the legislative process is that the Higher Education Bill has been complicated by an attempt to use it as a means of limiting the bus-ing of children from one place to another so as to break down the segregation of minorities in the United States.

The first need is to detach the anti-bus-ing amendment from the provisions of the bill which deal with higher education proper. Understandably, in the past five years, bus-ing amendment with an undertaking to look again at the United States. The proposal that funds for bus-ing should now be taken away quite understandably gives offence to liberal opinion anxious to see a rapid erosion of social barriers in the United States. It is only fair to add that the issue is so controversial that objective studies of its efficacy would be hard to carry out, but with five years of experience as a guide, there is at least a chance that it would now be possible to decide in what circumstances bus-ing is most effective and whether there are some circumstances in which quite different devices would be preferable. So is it entirely beyond the wit of Congress and those who wish to see an improvement of racial relations in the United States to head off the anti-bus-ing amendment with an undertaking to look again at the working of that programme in the light of the experience of the past five years.

The Higher Education Bill itself is also controversial. Luckily, the provision that students should be given a stipend of up to \$1,400 a year from federal funds has survived unchanged from last year's Senate Higher Educa-

tion Bill—this in itself could do a great deal to permit access to the universities by young men and women from disadvantaged families. And even though there might be advantages in a closer analogy with the British system, in which local authorities are responsible for spending the central government's money on student grants, in the long run the increased demand for higher education which the Educational Opportunity Grants will provide, and the federal vigilance on educational standards that will no doubt follow, will be a great benefit to all colleges and universities.

The difficulty has arisen over the way in which the federal government should spend money on support of institutions. Congress has devised for itself a formula which links the scale of institutional support to the amounts of money paid to students at each institution under the provisions for Educational Opportunity Grants and other grants, with a miniscule recognition of post-graduate teaching thrown in for good measure. By means of this formula, the federal government will be able in future to wash its hands of attempts to distinguish between good colleges and universities and the rest, a matter of great convenience for any Administration. The colleges themselves object to the way in which institutional grants will be weighted by the amounts of money paid out to their more needy students. But is not a better solution the development in the United States of the grant-giving bodies which now administer funds for university education in several countries elsewhere—the University Grants Committee in Britain is a good example? From this point of view, if the anti-bus-ing amendment can be detached from the Higher Education Bill, it would be best if Congress were to approve of the chief proposals on financing and were then to resolve that it would spend the next three years working towards a more permanent and satisfactory solution.

Dr Ehrlich's Backlash

SINCE his publication of *The Population Bomb* in 1966, Dr Paul Ehrlich has been one of the most constant, though not the most consistent, of the contributors to public discussion of what he calls the prospect of ecocatastrophe. Last week he turned up in Stockholm, a guest of the International Planned Parenthood Federation, to complain about American behaviour in Vietnam, commendably to draw attention to the gap between rich and poor countries, curiously to suggest that "man's assault on the vital systems is now increasing by about five per cent per year" and to plead for population stability. Two weeks earlier, he had identified for the gathering at Harvard to celebrate the centenary of the Arnold Arboretum, what he called an ecological backlash—a supposedly misguided attempt by natural scientists who are not "evolutionary biologists" to minimize predictions of disaster—with the usual proviso



"if things continue as they are". In the scrappy argument which has occupied the past few months, one of the most evident and most serious troubles has been the way in which complicated issues have been first simplified and then polarized so that the lay public is presented with a bizarre spectacle of unreasonable confrontation. At Harvard, Dr Ehrlich said that evolutionary biologists as a whole are in part to blame for having "failed to develop a broad evolutionary perspective among scientists in general". He is too modest, for he is personally responsible for much of the incoherence of the past few months.

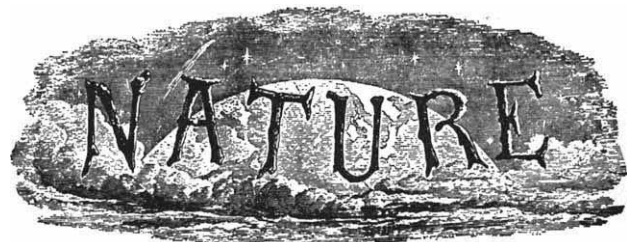
At Harvard, Dr Ehrlich said that the backlash which he has identified is based on three misunderstandings. The degradation of the environment does not consist of comparatively easily reversible sources of pollution such as air pollution, but in the way in which human activities, especially agriculture, are reducing organic diversity and thus limiting the capacity of natural and even artificial selection. He takes the view that the second source of misunderstanding is the belief that the process of demographic transition will not bring a sufficient measure of demographic stability to developing countries. And, finally, Dr Ehrlich complains that "the backslashers can't seem to comprehend the full meaning of the phrase exponential growth". And "this narrow perspective helps to generate the belief that rather minor changes can get us through the crisis. Install a smog control device here, a breeder reactor there, farm the Amazon basin, pass out contraceptives—but never promote a revolutionary change in the behavior of the entire species".

Dr Ehrlich's analysis of what he calls the backlash is, unhappily, erroneous. Thus, for example, he forgets that many of those who moderately protest at exaggerations of the potential consequences of air pollution are complaining not at him, but at others with whom he also disagrees. He is unjust to say that moderate opinion discounts the value of genetic diversity but the issue is for practical purposes one of degree and there is no reason why intensive agriculture, whether in the United States or in India, should by itself reduce genetic diversity in the world as a whole. To be sure, there are some benefits in agricultural regimes in which either the cultivation of a variety of crops or a clever rotation of crops can be devised to reduce the need for pesticides and artificial fertilizers, but there are economic penalties to be paid as well. The practical question is not how best to maximize genetic diversity but how to grow food most economically without causing long-term damage. In exactly the same way, the protests of demographers and others about extreme descriptions of "the population bomb" have consisted in declarations that his own predictions of the future, based on simple exponential calculations, are too simple, and are not intended to suggest that the demographic transition which has made Western Europe a relatively stable place can work the same effect elsewhere, in such a way as to achieve something like constancy of population in the developing world. The truth is that the population of the world will probably have doubled between now and the year 2010 and will thereafter continue to increase, but that the phenomenon of the demographic transition suggests not merely that a measure of stability will in due course be attainable, but also ways in which progress towards stability might be encouraged by means other than "passing out contraceptives". And on exponential growth, it is Dr Ehrlich and not his critics who suffers from misunderstanding. It is

simple arithmetic to calculate from the present growth rate that the world's population "will have a doubling time of 35 years if that rate remains constant", but moderate people are more concerned to identify the ways in which simple exponential calculations are invalidated by the ways in which growth rates change in the course of time under the pressure of events.

Dr Ehrlich's backlash is, therefore, not an obscurantist unwillingness to recognize problems that exist but rather a protest at the way in which he and others have made interesting and important problems appear too simple. Even the cause which he professes to support would be helped enormously if he were somehow able to recognize that one of the most urgent needs is to make environmental issues more susceptible to rational discussion. For the more distant future, there remains the possibility that the palliatives which he scorns may yet contribute to "a revolutionary change in the behaviour of the entire species". Certainly, the most gloomy of his predictions is that stability depends on a rapid revolution in the behaviour of the human species. Preoccupations in the past 2,000 years with the concept of original sin have made only a little headway in that direction. A more robust goal would be to use the governmental and international machinery which exists to solve problems which can be tackled now.

100 Years Ago



We now learn that Livingstone has reached Unyanyembé, that stores are being sent up to him as rapidly as possible in charge of his son, and that he will march southward to explore this Ruaha or Lufiji river, this mighty outlet of the great system of waters that he has discovered, with its lofty cliffs and alleged natural tunnel. Thus, for the third time, all fears have been dispelled, again we get a glimpse of this true knight-errant, and again we find him steadfastly working at the task he set himself to do six years ago, and which he will not abandon until it is finished. This last section of his labours will comprise the complete discovery of the great basin of the Tanganyika, including the collection of accurate information respecting its limits, its varied climates, its productions and capabilities and people, its rivers and lakes, and its outlet to the Indian Ocean. The addition to geographical knowledge will be enormous, and we may well hope that this knowledge will be the means by which a new country will hereafter be opened to European enterprise, and the object of Livingstone's life be attained. If he dies in the midst of his discoveries he may well be envied, for a nobler and more glorious end can hardly be imagined. If, as we all hope and as is more likely, he is spared to return home, and perhaps to watch in his old age the progress of the mighty work which he is now initiating, he will receive a welcome from his countrymen such as few have experienced and fewer still have so justly earned.

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OLD WORLD

Another Catch

HAVING already enticed Dr Renato Dulbecco from the Salk Institute (see *Nature New Biology*, **232**, 99; 1972), the Imperial Cancer Research Fund announced last week with understandable elation that Dr John Cairns, currently a member of the Cold Spring Harbor Laboratory and formerly director, will be joining the staff of the ICRF in the late autumn of this year to be head of its Mill Hill laboratory. (Dr Dulbecco, incidentally, is due in London in September.)

With these two outstanding successes in international recruiting under its belt, the ICRF, on paper at least, has clearly established itself as one of the pre-eminent European laboratories for cancer research, with strong if informal links with both the Salk Institute and Cold Spring Harbor and, moreover, an independent financial position which today must be the envy of many a laboratory on both sides of the Atlantic. Whether, of course, the ICRF will now be able to exploit its unique advantages in a way which will benefit cancer patients and thereby justify its wealth of cash as well as talent remains to be seen.

Cairns, it hardly needs saying, is a doyen among investigators of DNA replication; in 1963, he provided visual proof, autoradiographs, of the circular form of the *E. coli* chromosome and proposed a model to account for the replication of circular chromosomes which has withstood the test of time, while more recently he isolated mutant strains of *E. coli* which, despite carrying nonsense mutations in the structural gene for the Kornberg DNA polymerase I, continue to multiply. This discovery threw the question of the biochemistry of DNA replication back into the melting pot from which it has yet to emerge.

Cairns and a few colleagues will apparently continue their investigations of DNA replication in bacteria once they have settled in at the ICRF outpost at Mill Hill which is literally in the shadow of the MRC's National Institute for Medical Research. The staff of the National Institute will surely be delighted that the ICRF has succeeded in attracting Cairns to its Mill Hill laboratory, of which he will act as chairman, for they will have ready access to him. The same cannot unfortunately be said of the great majority of the ICRF's own staff who are housed

in central London in Lincoln's Inn Fields: Cairns is not, however, a stranger there, for until the end of January this year he was a sabbatical visitor. Neither is he a stranger to animal virology. In the 1950s, he worked as a virologist successively at Melbourne at the Virus Research Institute at Entebbe, Uganda, and for several years in Fenner's laboratory at the Australian National University in Canberra before he moved to Cold Spring Harbor and immersed himself in the problems of DNA replication in *E. coli* and of fund-raising.

To its credit, the ICRF has accepted the eminently sensible argument that

there is little hope of understanding the mechanism and control of DNA replication in animal cells, which is surely central to an understanding of cancer, until these processes have been elucidated in such comparatively simple organisms as bacteria. The fund is therefore quite prepared to support Cairns's research, which may at first sight seem irrelevant to curing cancer. Both space and funds are, however, available to allow the development of two or three additional research groups at Mill Hill. It is confidently anticipated that these will be more obviously and directly related to the disease of cancer in man.

EDUCATION

Conflict and more Conflict

THE storm in the Open University's tea cup over exemptions for students holding Higher National Certificates has blown over. But the Institution of Civil Engineers and the university are heading for conflict over recognition of the university's technology courses.

Mr Colin Russell, chairman of the credit exemptions committee of the Open University, pointed out at the end of last week in a letter to *The Guardian*, which a few days earlier had carried the first report of a possible conflict between HNC holders and the university, that "there is no question of the Open University downgrading the HNC".

Six credits are needed for a degree at the Open University, and the university will allow a student up to a maximum of three exemptions—basically one for each year of full time study, or equivalent after A-level. Mr J. G. Woodward, secretary of the university's credit exemptions committee, said earlier this week that an HNC is considered by the university to be worth one general credit exemption—even though it usually takes two years of study to obtain the qualification—and that the university has no plans to change the system, contrary to newspaper reports.

The misunderstanding has arisen from the university's practice of allowing a further credit exemption if a student has three endorsements to his Higher National Certificate obtained by studying further subjects. Mr Russell points out in his letter to *The Guardian* that the Open University does not automatically accept three endorsements as a qualification.

This particular dispute has arisen be-

cause the Open University has decided that the two HNC courses in industrial administration should count only as one endorsement, although by so doing it has run counter to the advice of the joint committee for HNCs which has gone on record as saying that the courses deserve two endorsements. The Open University says, however, that this is its own decision, and that for its requirements the two courses are only worth one endorsement. "There is no blanket policy of allowing exemptions for endorsements".

The particular endorsements in question are held by only about 100 of the 18,000 students of the university who have submitted claims for exemption, but this conflict represents only the tip of the iceberg, as disagreements between the Open University and the professional institutions run much deeper.

There seems, for example, no hope in the immediate future that the Institution of Civil Engineers will recognize the technology courses now being offered by the Open University as a qualification towards professional recognition. The institution this week insisted that it was up to the university to submit its syllabus for approval to the institution, while a spokesman for the university said that the university had no intention of doing so.

A spokesman for the Institution of Civil Engineers said this week that all engineering courses at the new universities were accepted by the Council for Engineering Institutions as being of the necessary standard when the new universities were set up—without the ICE or the other institutions individually studying the syllabuses.

NUCLEAR POWER

Canada Candu?

SHOWING scant respect for the already furrowed brows of Britain's ministers at the Department of Trade and Industry, Canada has thrown into the ring yet one more option for the third generation of nuclear power plants.

Which reactor type Britain should choose to follow the as yet non-operative advanced gas-cooled reactors (AGR) has been exercising the minds of the nuclear power industry in general, as well as the DTI (in the shape of Mr Peter Vinter and his thermal reactor review) in particular, for more than eighteen months. A decision has been expected for some weeks now, and successive rumours have suggested that each in turn of the reactor types under consideration is the one most likely to be chosen.

Essentially the choice lies between British reactors, which means more AGRs, completing the development of either the steam-generating heavy water reactor (SGHWR) or the high-temperature reactor (HTR) and of buying American light water reactors.

The Canadian proposal is that Canada will provide Britain with full details of one of the world's most successful nuclear power projects—the Candu system in use at the Pickering station at Toronto—in return for collaboration on heavy water reactors, which means in practice collaboration over the SGHWR.

The logic behind the Canadian offer is not difficult to see. The Pickering station—four 500 MW sets—has come into service promptly and reached full load in record time—Pickering III attained full load eighteen days after going critical, a record that the British nuclear power industry might well envy. The reactor is a heavy water type, not very different from the SGHWR but using a natural fuel, and the Canadians hope that their knowledge of pressure tubes and successful construction can be combined with Britain's knowledge of enriched uranium fuels to produce a world-beating formula—at least until fast breeders become a commercial proposition.

The Canadian offer was announced in Ottawa by Mr J. L. Gray, president of Atomic Energy of Canada Ltd, but in London it has evoked more enthusiasm from the Canadian High Commission than from Whitehall. The Department of Trade and Industry was willing to admit this week that Sir Antony Part, permanent secretary at the DTI, had received a letter from Mr Gray and added that the letter would no doubt be considered by ministers in coming to their decision, but beyond that the DTI would not go.

Mr J. L. Orr, Scientific Counsellor

at the Canadian High Commission, however, said that Canada is willing to explore any level of cooperation with Britain, from an exchange of research information to full industrial collaboration. Canada, Mr Orr said, has its eye on export markets in South America, Australia and South Africa in making the proposal because it believes that the use of enriched fuel could make the heavy water reactors sufficiently cheap to compete abroad against the American light water reactors.

On the face of it the Canadian offer has its attractions. The Candu system has proved itself technically, if not yet economically, and the combined operating experience of the Canadians and British knowledge of using enriched fuels in the prototype SGHWR at Winfrith, might well produce a commercially viable system, although it remains to be seen if it would be competitive when set against the American light water reactors. On the other hand, there are no doubts about the safety of the heavy water reactors as there are about the American machines.

But the initial British reaction has been cool. It is early days yet, and none of the organisations likely to be involved in such a project has any comment to make, but one of the commonest reactions among people in the industry is that Britain has the SGHWR anyway should Vinter and the government choose a pressurized water reactor. Nevertheless, there is no denying that Canadian experience of actually building and operating Candu commercially would be an advantage—scaling prototypes up to commercial plant size has not always been a happy experience.

Whatever the outcome, it is at least one more alternative for the government to mull over before coming to its final decision. The chief reason for the delay, however, may well not be the difficulty in choosing between the various systems in which Britain has already invested. Since Vinter set out on his enquiry, the government has had to reconsider the future of nuclear power in relation to the large and increasing finds of North Sea oil, and in relation to the future of coal, particularly following the miners' strike earlier this year.

EUROPEAN SCIENCE

Foundation far ahead

A EUROPEAN policy for industrial innovation is "still a subject for the future" according to Mr Henrich van Molthe, director of studies and methods for technological development at the European Economic Commission. Speaking at a conference on industrial

innovation in London last week, Mr van Molthe said that a policy was nonetheless under consideration and that several points are to be put to ministers shortly. Europe, he said, has never had an innovation policy and the existing EEC agreement contains nothing about research and development; to rectify this the following proposals may be put to the ministers of the community.

- A European Science Foundation should be established. The foundation should promote cooperation on fundamental research between the universities and research establishments, encourage the flux of personnel between the two, and organize the shared use of big science facilities.

- The community should grant research contracts in materials science and environmental pollution, over and above anything that COST (European cooperation on scientific and technological research) may decide to do. Such work would help produce comparable standards of environmental control throughout Europe — for example on lead in petrol.

- The EEC should be able to put forward up to half the finance for medium sized innovation projects by small companies, at a low interest rate—say 3 per cent per annum—the operation to be controlled by the European Investment Bank, which would also help support companies in the production phase that follows the research and development.

- There is also the tentative possibility of forming a club of European venture capital companies combined with the European Investment Bank to ease the supply of venture capital and to underwrite larger and even riskier projects.

Mr van Molthe stressed that these ideas are not yet proposals. He also went on to point out that while the amount of research and development undertaken in the EEC had risen sharply in the past ten years, "this increase cannot be expected to go on forever". He predicted that the increase would continue for a few more years but that this would be followed by a period of levelling off, "which will put an end to the easy time for science money". The trend now evident in the United States towards more research on environmental and social matters will be followed in Europe and thus less money will be available for industrial innovation.

Patterns like this, Mr van Molthe added, call for long term planning and reassessment of economic and social aims. An innovation policy, along the lines outlined above, could help Europe through the problems of reassessing its economic and social aims, according to Mr van Molthe.

Politics, Bureaucracy and the Environment

by our Special Correspondent

Stockholm, June 10

THE first week of the United Nations Conference on the Human Environment has turned out to be less placid than the organizers had expected. In spite of two years of brooding by the Preparatory Committee on the details of Mr Maurice Strong's Action Plan, several of the specific proposals have become bones of contention. Several speakers at the non-stop talk show which has constituted the plenary session's proceedings in the first week, notably those from African countries, have made vigorous protests at the pre-occupation of advanced countries with the environment but not with foreign aid. The internal politics of the United Nations have frequently broken surface, and there has been a small foretaste of the drubbing which UNESCO will be given by its General Assembly in the autumn. Both the French and the Chinese have had to eat humble pie for continuing to test nuclear weapons in the atmosphere. And, worst of all for Mr Strong and his organizers, the Chinese have succeeded in arranging a detailed discussion of the Declaration on the Human Environment which had been designed as a document to set the conference rooms echoing with loud huzzahs.

Among the speakers at the plenary meetings, Mr Robert McNamara, President of the International Bank for Reconstruction and Development (the World Bank), stood out for what he had to say about the relationship between the need for economic development and the preservation of the environment. Mr McNamara's developing world is a bleak place. "Hunger and malnutrition are sapping energy, stunting bodies, and slowing minds. Illiteracy is locking out learning and paralysing opportunity. Unemployment is not only robbing men of the minimal means to make their way, but leaving their pride broken and their ambition atrophied. Wholly preventable diseases are injuring infants, killing children, and ageing adults long before their time." Yet existing development programmes "are not significantly reducing the poverty which shapes and limits these lives" partly because developing countries are slow to reduce their own social and economic inequities and because developed countries are slow to reduce the gap between their own opulence and the penury of the rest of the world. Development, he said, cannot succeed unless these distortions, national and international, are removed. Yet without economic growth "a poor country can only remain poor"

while economic growth in developed nations is necessary if they are to play a part in "the achievement of a level of life in accord with fundamental human dignity". The dilemma, said Mr McNamara, is how to reconcile this need with the proper management of the environment. He said the first need is for a better understanding of the dilemma, amending "in a more scholarly manner the alarmist views of some who are deeply persuaded of the problem but unaware of the full complexity of its elements". Mathematical modelling is useful, but it is only as useful as the validity of its assumptions and the comprehensiveness of its inputs. Evidently the Club of Rome has failed to make one influential friend.

One danger of oversimplification, said Mr McNamara, is that the developing peoples of the world are faced with the fearsome prospect of being asked to forgo development so as to preserve the disproportionate consumption of the rich, and are rightly indignant as a result. Yet there is no evidence that economic growth will necessarily impose an unacceptable burden on the environment.

Mr McNamara said that since the World Bank began, in 1970, to make an environmental assessment of each new development project, it had turned out that the environmental hazards of new developments could be reduced either at no cost or at a cost so moderate that those borrowing money for them were entirely agreeable to paying extra. He feared that some rich countries, "under the influence of doomsday alarmism", may be tempted to impose "unilateral and unreasonable road blocks" on the poor countries' desperate need to develop.

What is to be done? The latecomers in development may avoid needless mistakes but they cannot forgo industrialization and technical development—that would mean stagnation. If the twin objectives of development and the preservation of the environment are not attained, the cause will be a failure of political will and social responsibility, so there is a need for more development assistance and the removal of discriminatory trade barriers. And in the last resort, the world must recognize that poverty is the one hazard which can injure not only the habitat and health of human beings but their spirit as well.

The other striking contribution to the plenary debate this first week came from Dr Sicco Mansholt, president of the European Commission, who echoed much of what Mr McNamara had to say but who is nevertheless known to be fonder of the Club of Rome. In the

past 20 years, in spite of endless international conferences and new resolutions, poverty has not been eliminated—the rich get richer and the poor poorer. The third UNCTAD conference demonstrated that the world is not yet able to remedy this situation. On the environment, the Stockholm conference was in a sense a continuation of the discussions at UNCTAD in Santiago two months ago. The problem is how to reconcile an appreciation of the finite character of the world with a solution of obvious social evils.

Dr Mansholt came out in favour of compensation for developing countries to offset such disadvantages as might be occasioned by environmental protection measures in the well-heeled world. He said that all countries and the United Nations would have to work out ways of remedying the disparity between rich and poor nations within the finite limits of the real world and told, as a cautionary tale, the story of how the European Communities had set out in 1965 to make their public investment grow at eight per cent a year, twice as quickly as the planned rate of growth of GNP. In the event, GNP had grown at five per cent a year but public investment kept exactly in step and necessary investments were sacrificed in the struggle against inflation. If such a sorry tale could be told of Western Europe, how much more difficult it was bound to be to carry through a vast programme of public expenditure for the improvement of the whole environment.

The chief delegates of countries such as the United Kingdom and the United States have been at pains to emphasize their wish to see practical consequences flow from Stockholm. Mr Peter Walker, the Secretary of State for the Environment, was especially strong on ocean dumping, cleansing rivers, monitoring and technical assistance, and went so far as to promise a British contribution to the \$100 million fund for the continuation of the United Nations Programme on the Environment. He announced a study of the long-term trends "in the factors affecting the human situation", with a dash of mathematical modelling. It is not clear precisely what Mr Walker meant by saying that economic growth must take a new direction or whether he had consulted the Chancellor of the Exchequer on the subject.

For the United States, Mr Russell Train, chairman of the Council on Environmental Quality, urged support for a continuing 27-nation commission of the United Nations Economic and Social Council to guide the United

Nations Programme on the Environment. Mr Train urged action on such things as ocean dumping and the preservation of the whale by means of a ten-year moratorium on hunting. The force of his public contribution to the conference was more than a little blunted by his unnecessarily touchy reaction to a passage in the speech by Mr Olof Palme, the Prime Minister of Sweden, who referred indirectly, earlier in the week, to American military operations in Vietnam. Mr Train will no doubt learn in time that criticisms like these are not adequately met by the complaint that they have been made in the wrong place.

In the event, Mr Train has not so far responded to more direct criticisms than that of Mr Palme—that of the head of the Nigerian delegation, Professor Adebayo Adedeji, for example, who also wrung his hands over the continuing economic and political disunities that make a nonsense of the conference slogan "Only One Earth".

The reopening of discussion of the Declaration on the Human Environment, accepted with a brave but wan smile by Mr Maurice Strong on the grounds that it was "democratic", is only to have been expected, but the opposition of the delegations of the United States and Canada to the Chinese proposal was not carried to a vote this week. In their mild plea that the question should be reopened, the Chinese argued that the document would have greater force if everybody had been consulted about it and they volunteered the information that on the whole they thought the declaration was a worthy document. The trouble, which the organizers should have anticipated, is that the document is also so much wider in its scope than the Action Plan which Mr Maurice Strong has devised that it is bound to raise all kinds of contentious issues. The declaration that "Man has the fundamental right to adequate conditions of life" is, for example, an invitation for a discussion of how national communities should be organized, economically and otherwise, and it is naive of the organizers to have thought that the declaration should speak out against the testing and use of modern weapons but that the conference itself should have nothing to say on the subject. Only the next few days will show whether the draft declaration will emerge in recognizable form from the working party now in charge of it or whether it will emerge at all.

Complaints about nuclear testing have come from all quarters, some of them surprising. The chief delegate of New Zealand, Mr David MacIntyre, fiercely attacked "the double standard" of certain countries on the environmental hazards of continued testing and

said that he and his countrymen were deeply resentful of the continued use of the South Pacific as a testing ground by the government of France. New Zealand and eight other countries took up their cause in one of the technical committees, with the result that the record of the conference will include a fierce declaration against continued testing. The Peruvian delegation had what may have seemed at the time to be an unexpected success on Friday by securing virtually unanimous support for a resolution condemning atmospheric nuclear tests—this is the point at which both the French and Chinese delegations hung their heads or, more accurately, made thin excuses to the conference.

The outlines of the conference's recommendation for continuing UN organization are already apparent, subject to final approval by the General Assembly in September (when the Russians will have their say for the first time). Schemes for constructing an environmental agency along the lines of UNCTAD, which has its own governing body and which can form links with non-governmental organizations but which also reports to the General Assembly, have apparently been discarded. The developing countries hope that such a device would make it easier to ensure that compensation for the effects of environmental policies on the trade of developing nations was paid out on time, but even developing nations must now be disenchanted with UNCTAD. The most likely outcome of the second week of the conference is a permanent commission of the Economic and Social Council of the United Nations making environmental policy which is administered by a secretariat (of which Mr Maurice Strong is likely to be the first head), the wheels being oiled by the \$100 million which seems to be the most that there will be for the first five years.

How will the money be spent? One tangible proposal is that there should be an international referral service, the details of which are likely to be worked out by an expert committee. The British delegation has been articulate in its view that the proposed service should be flexible, not so much a data centre as a means of putting potential users of information in touch with potentially useful sources. The scheme for a worldwide system for monitoring the condition of the environment is likely to emerge unscathed from the committee meetings in the second week of the conference, but it is not yet entirely clear precisely how the interested agencies of the United Nations, especially WMO and WHO, will be involved. There are specific schemes for the development of soil mapping, forest

management and the safe (and perpetual) custody of wildlife species (including microorganisms) which would in practice be administered by individual agencies of the United Nations.

In retrospect, the organizers probably regret that their much vaunted Action Plan has been so detailed. Not merely has this made it necessary for committees to scamper, often without discussion, through a huge agenda, but it begins to be apparent that many of the recommendations have not yet enjoyed the benefit of full technical discussion, economic priorities are undetermined and some recommendations are frankly half-baked. Since it is unlikely that recommendations like these would ever carry anything resembling the force of law without approval by the General Assembly, it might have been much better if this conference had been presented not so much with an action plan as with a well worked out scheme for environmental coordination internationally and with a promise that specific recommendations would follow later.

The abatement of marine pollution, every delegation's favourite cause, has been immensely preoccupying for a different reason. In the past two years, several maritime countries have come near to negotiating an international convention to regulate ocean dumping. The British delegation eventually won its case for an international conference on the subject in London before November, with the prospect of signature of an agreement before the end of 1972. Waiting for the General Assembly to have its say was plainly unacceptable to the maritime powers, but many developing countries, Brazil especially, were anxious to use existing machinery, the International Oceanographic Commission in particular. (This is a pensioner of UNESCO and is now, at the instruction of the Stockholm conference, to be made stronger than UNESCO has so far allowed.) Whaling was also a contentious issue—Japan has stood out against a ten-year moratorium, and no doubt the Russians will follow suit later in the year.

Sideshows continue. The Environmental Forum daily washes its hands of the conference, apparently oblivious to what people like Mr McNamara have been saying. Dr Paul Ehrlich visited a contraceptive shop for the benefit of photographers and was snatched away from one press conference to another which his sponsors had arranged elsewhere. Mr Edward Goldsmith, editor of *The Ecologist*, has said "the idea that economic growth can cure disease is unsound on scientific principles. . . . This idea is the product of only one society—a society on the verge of extinction".

NEW WORLD

Dim Light at the end of the Tunnel

by our Washington Correspondent

UNIVERSITY administrators and college presidents have a right to feel annoyed at the shoddy treatment they have received from some members of Congress. Although faced with a financial crisis that is forcing many institutions of higher education to restrict student enrolment, abandon courses and even close their doors, the academic community has had to wait for several months while a complex bill designed to provide financial assistance to higher education has been delayed by a fight over the merits of desegregating schools by bus-ing children from one district to another. The Higher Education Bill was, however, finally passed by Congress last week, and although it represents a radical departure from established traditions in the relationship between the federal government and the colleges, it has by no means won the hearts of the entire academic community.

The version of the bill which came out of a conference committee last month and which was passed by Congress last week was much closer to the bill passed by the Senate in August last year (see *Nature*, **232**, 518; 1971) than to the measure which was passed by the House of Representatives a month or so later (see *Nature*, **234**, 65; 1971). Instead of providing federal grants to each college solely on the basis of the number of students enrolled, as the House of Representatives and the higher education lobby had originally wanted, it provides the grants chiefly on the basis of the number of federally-supported students from low income groups who attend each college. The bill also establishes the right of every student to receive up to \$1,400 a year from the federal government in the form of a Basic Educational Opportunity Grant (BOG). The actual amount of the grant would be based on parental income, in much the same way as university students in Britain are financed by grants from local education authorities.

Both measures represent landmarks in the history of higher education in the United States, for the federal government has previously steered clear of providing direct, across-the-board grants to colleges to do with as they wish, and there is at present no scheme such as the opportunity grants to ensure that no qualified student is barred from attending university solely because of financial hardship.

In spite of the historic nature of the bill, and the fact that it could channel \$18,500 million into the universities and colleges over the next three years, however, the academic community is strongly divided about its merits. The higher education lobby in Washington in fact strongly supported the idea of institutional grants based solely on the number of students enrolled in each establishment, but it has remained lukewarm towards the suggestion that institutional grants should be tied to the number of federally aided students at each institution.

A measure of the division in the academic community is the fact that higher education lobby groups, such as the American Council on Education, were slow in announcing their opinion of the conference report and, once formed, their support of the measure was barely tepid. A letter from Mr

Roger W. Heynes, president of the American Council on Education to presidents of member colleges, for example, expressed "disappointment that the conference has rejected the broad principle that the federal government should provide general support to all institutions on the basis of the number of students educated. Nevertheless, the bill does provide general support on the basis of federally assisted students, and this (the members of the board of ACE) view as at least an initial step towards what we believe should be a federal responsibility".

Proposed by Senator Clairborne Pell of Rhode Island, the idea of tying institutional support to the numbers of needy students at each institution will probably cost about \$1,000 million a year. Its design, apart from providing much needed finances to colleges and universities, is to make institutions of

EDUCATION FINANCES

More Trouble Ahead

ANY doubts that there may be about the gravity of the funding crisis in American higher education should be dispelled by the latest report from the Carnegie Commission on Higher Education. The report suggests that if the growth in annual expenditure of institutions of higher education continues in the 1970s at the same rate as in the 1960s, an extra \$26,000 million will have to be found by 1980 just to keep all the institutions running.

The commission's report, to be made public this week, sets out a programme for meeting this shortfall that would make academic administrators in Britain throw up their hands in horror. (Indeed, the vice-chancellors did just that when Mrs Shirley Williams, then the minister responsible for higher education in the Labour Government, put forward some of the same suggestions three years ago.) What the commission suggests is that 60 per cent of the funding gap should be made up from new funds from state and federal government, but that the institutions themselves should be prepared to reduce their expenditures to close the gap.

Higher education costs can be cut, the commission suggests, in two ways. First, the total number of years of student instruction should be reduced by streamlining courses and by reducing the number of "reluctant attenders"—although the latter reduction is outside the control of the institutions themselves—and, second, more effective use should be made of existing resources.

Among the commission's prescriptions for using resources more effectively is a halt to the creation of any new PhD courses, except in very special circumstances, and even more concentration of PhD training and federally supported research in fewer institutions. Indeed, New York State has already put this suggestion into practice by declaring a moratorium on new PhD courses last year. The commission also believes that campuses and departments should reach a minimum effective size, and that the student-faculty ratio can be cautiously raised, in spite of the fact that there has been considerable erosion of the ratio during the past few years. More educational experiments off campus, such as the open university experiment and credit by examination, should be tried out, and institutions should set up consortia or even mergers.

The commission also notes that the tight job market for faculty members will tend to keep salaries down, and that the trend towards enrolment in two-year colleges will result in some saving.

higher education more willing and more able to enrol needy students. Combined with the fact that students from low income families will be eligible for the BOG grants, the effect of the bill, if it is fully funded, should be to increase the accessibility of higher education to financially handicapped students.

In detail, the institutional support grants contained in the conference report will be parcelled out according to a complicated formula. Forty-five per cent of the funds allotted for support grants will be given on the basis of the number of students who receive the new Basic Educational Opportunity Grants, another 45 per cent of the money will be shared out according to the total amount of money received by students at each institution from the old educational opportunity grants, work study and National Defense Educational Assistance loans, and the final 10 per cent will be distributed on the basis of \$200 for every postgraduate student at each institution.

Part of the opposition to the measure is based on the fact that it might work against students from middle-income families, but another criticism that has been voiced is that what is needed at present is immediate and uncomplicated federal relief from financial ills.

Many college presidents have argued, in their letters to Mrs Green and in other public statements, that the conference report should be turned down by Congress, that another bill simply continuing federal funding in 1973 at the same level as in 1972 should be rushed through, and that the provisions of the Higher Education Bill should be thought out more thoroughly and incorporated into another bill which would be introduced later. Opponents of the conference committee's institutional aid formula also point out that since the amount of money is contingent on other provisions in the bill, unless all the bill's proposals are fully funded—which is unlikely—the total amount of money available for the desperately needed institutional grants will be reduced.

Although the institutional aid provisions of the bill go to the heart of the federal government's relationships with the higher education community, it is the antibus-ing provisions that have stirred up the most public dissent, and which placed the whole bill in jeopardy. Antibus-ing amendments clearly have no place in a measure dealing with higher education, but the bill was used as a convenient vehicle for opponents of bus-ing to force through Congress as quickly as possible a measure that would put a halt to court-ordered desegregation.

Leader of the move to tack the antibus-ing amendments on to the House

bill was Mr John Ashbrook, the arch-conservative from Ohio who has been running against President Nixon for the Republican presidential nomination because he believes many of Nixon's policies are too liberal. Ashbrook and several antibus-ing supporters tacked an amendment on to the higher education bill when it was first passed by the House of Representatives. The amendment would have prevented federal courts from ordering schools to be desegregated by bus-ing students from one district to another.

The chief problem for the higher education provisions of the bill was that bus-ing has emerged as one of the most highly charged issues in this election year. There is reported to be a strong public sentiment against using forced bus-ing of children to achieve racial balance in the public schools. George Wallace rode the issue with much success throughout his election campaigning, and President Nixon preserved his electoral base by sending to Congress a bill which would have placed a moratorium on all court ordered bus-ing.

The bill that emerged from the conference committee was less stringent than the hard-line measure passed by

the House of Representatives, although it went further than the amendment tacked on by the Senate. Essentially, it provides that when a federal court orders bus-ing to achieve racial balance, the local groups need not comply until their appeals have been exhausted. The existing law, based on a 1969 decision of the Supreme Court, is that bus-ing should begin immediately it is ordered by a federal court. In the event, the House of Representatives passed the bill by a vote of 218 to 180.

What will the White House do with the bill? It seems likely that the measure will be signed by President Nixon without too much delay, because although its bus-ing provisions do not go as far as he originally wanted, effectively the measure gives him the moratorium he requested.

The higher education community is therefore likely to get the financial shot in the arm that it has been seeking for a long time. Unfortunately, however, because of the delay caused in part by the antibus-ing fight, and in part by the differences in philosophy over institutional support, the money will arrive in the universities too late to affect planning for next year.

GRADUATE STUDENTS

Enrolment Sags

by our Washington Correspondent

THE shrinking job market, cutbacks in enrolment by private universities and the scarcity of funds for student support caused graduate enrolment in science departments to decline by 5 per cent between 1970 and 1971. This finding, the fruit of a survey of nearly 3,000 science departments conducted by the National Science Foundation, is further evidence of the downward trend noted in 1970, when graduate enrolment declined by about 2 per cent, and the reduction is heaviest among part-time students.

Particularly affected are the top twenty institutions—those that receive the most money for research and development from the federal government and which were awarded the greatest number of NSF fellowships.

Graduate enrolment in these institutions declined by 8 per cent between 1970 and 1971. And it seems that private universities have been forced to cut back their graduate intake rather more drastically than have the public universities—the respective declines are 6 per cent and 1 per cent.

One reason for the decline that is evident from the NSF survey is simply a lack of support for graduate students. The number of students supported by fellowships and traineeships in 1971 dropped by 10 per cent compared with the previous year, and while the federal government supported some 37 per cent of all graduate students in 1969, it supported only 32 per cent in 1971. Moreover, the full impact of recent reductions in federal traineeships—particularly those administered by the NSF itself and by the National Institutes of Health—will not be felt until this year.

Other findings from the survey include:

Table 1 Per Cent Change in Graduate Enrolment in Doctorate Departments, by area of Science and Enrolment Status, 1969–71 *

Area of science	Total		Full time		Part time	
	1969–70	1970–71	1969–70	1970–71	1969–70	1970–71
Total	–0.7	–2.9	†	–1.5	–3.1	–7.9
Engineering	–1.7	–5.7	2.6	–2.0	–8.0	–11.8
Physical sciences	–3.5	–5.6	–3.4	–4.3	–4.1	–14.7
Mathematical sciences	0.3	–5.8	1.3	–4.3	–3.2	–10.9
Life sciences	1.2	–1.1	0.4	0.1	8.1	–10.0
Psychology	1.5	4.2	1.2	4.8	3.8	–0.2
Social sciences	0.5	0.4	–0.6	–0.9	4.0	4.5

* Data are based on 2,579 doctorate departments reporting in autumn 1969, 1970, and 1971.

† Less than 0.05% change.

NEWS AND VIEWS

Low Frequency Radio Signals from Extensive Air Showers

COSMIC rays of very high energy, say greater than 10^{18} eV, are of considerable astrophysical interest. In the first place, diligent effort has failed to reveal any anisotropy in the flux and their sources remain speculative. Even if a specific object were identified, there would still be the problem of the mechanism by which an energy of about a joule can be imparted to a single particle. Furthermore, once the energy exceeds a few times 10^{19} eV the primary radiation should interact readily with the microwave background radiation and be strongly attenuated in even quite a short journey (by galactic standards) from source to detection. Measurements of the flux of such primary radiation may, therefore, indicate how universal the microwave background is.

These particles are, unfortunately, very rare: for example, primary particles of energy greater than 10^{18} eV occur at a rate of roughly one per square metre per millennium. The detection of such a particle is only possible because it generates a cascade of secondary particles in its passage through the atmosphere which spread out as they go over an area several hundred metres wide. It is therefore possible to infer from a few samples taken over an area of about this size the existence (and energy) of the parent primary by observation of the secondary, air shower, particles. For detection of the rarest particles of very high energy the effective collecting area must be increased substantially, to many square kilometres, and detector arrays of the necessary heroic proportions are now operated in Britain at Haverah Park, in Australia by the University of Sydney and at Yakutsk in the Soviet Union.

The great size of the detector required for an effective study of the energy region above 10^{19} eV has prompted a search for alternative and less costly methods of detection. One such method would make use of the radio pulse generated by the air shower in its passage through the atmosphere. H. R. Allan has recently reviewed the present status of studies on radio air showers (*Progress in Elementary Particle and Cosmic Ray Physics*, 10, 171; 1971) and comment on some aspects of recent experimental work at low radio frequencies has appeared in these columns (see *Nature*, 232, 14; 1971).

In a nutshell, it seems likely that a detecting array using radio techniques would only be practicable using frequencies of a few MHz or lower, for at higher frequencies radio signals are detectable only over a limited area in the middle of the shower. The lateral scale of the radio signals, however, is expected to increase with decreasing frequency. Such measurements as have been obtained at low frequencies suggest that the radio field strength is large, although the high level of background interference at these frequencies complicates the observations. On page 384 of this issue of *Nature*, Allan extends his theoretical analysis of the radio signals into this interesting low frequency region.

There are two equivalent ways of approaching such a calculation: the first is to solve Maxwell's field equations, putting in source functions based on realistic models for the development of the shower in the atmosphere; the

second is to make use of an approach formulated by Feynman and described in his celebrated "lectures". In essence, this is an action-at-a-distance formulation in which the electric field intensity at a point is computed from the apparent motion of the charges responsible for generating it. It is the second approach which Allan has exploited with a good measure of success in the past to predict the properties of radio signals at frequencies above 30 MHz. He now finds that when the same methods are applied to the calculation of field strengths at frequencies around 5 MHz, the computed values fall short of the observed ones by a couple of orders of magnitude; even an extravagantly generous upper limit falls short by at least an order of magnitude.

The virtue of Allan's method of calculation is its elegant, transparently physical simplicity: it is difficult to see how it could be wrong. The measurements of low frequency fields have been carried out by three independent groups on three different continents. As Allan says, "The contradiction is complete". The contradiction will now presumably stimulate a search for a new mechanism by which the low frequency signals are produced and at least a little soul-searching by the experimenters.—From a Correspondent.

Inhomogeneous Earth

IDEAS about the formation of the Earth's core—the latest of which are discussed by Anderson and Hanks on page 387 of this issue of *Nature*—have proliferated so much in recent years that the average reader, perhaps not intimately concerned with the problems involved, may be forgiven for wondering who now to believe. The essential difficulty is, of course, that the formation of the core is so far away in both time and distance that Earth scientists must be content with intelligent speculation and only the minimum of fact, the idea being to try to formulate the simplest, most plausible hypotheses which do not actually conflict with the few hard bits of information which exist. The result is a welter of different hypotheses, each of which is based on geochemical and geophysical evidence which is often quite detailed but circumstantial rather than observational (for example, the results of meteorite or laboratory studies rather than investigations of Earth materials *in situ* and none of which is entirely satisfactory).

But in spite of the apparent confusion, it is possible to discuss some important trends in the evolution of ideas concerning the Earth's core, ideas which must inevitably be bound up intimately with the wider problem of the origin of the whole Earth and the solar system. It is now many years since the belief that the Earth formed in high temperature conditions gave way to the opposing theory involving low temperature accretion from particles which on average probably represented a roughly chondritic composition. For such accretion to have taken place at low temperature, however, the speed of the process would

have had to have been slow enough to enable the gravitational potential energy to be radiated away, a condition which is frequently interpreted in terms of an accretionary period of about 100 million years. The cold accretion theory then usually goes on to say that heating of the Earth by long-lived radioactive isotopes took place later, giving rise to the differentiation which resulted in the formation of the core. In short, core formation may well have taken place some considerable time after accretion (that is, after the formation of the Earth itself) and may even be continuing today.

This is what may be regarded as the basic conventional view of core formation; but there is an important variation on it which, ironically, marks a return to a "hot origin" theory, though in quite a different sense than that intended before the acceptance of accretion. The idea here is that accretion took place too rapidly for the gravitational potential energy to be radiated away effectively, that the accretion temperature was thus high, and that the conditions necessary for core formation obtained more or less at the time of accretion. The first proponent of this view was probably Ringwood (*Geochim. Cosmochim. Acta*, **20**, 241; 1960) who supported it on geochemical grounds, although it was later taken up by Hanks and Anderson (*Phys. Earth Planet. Interiors*, **2**, 19; 1969) and, more recently, received experimental support from Oversby and Ringwood (*Nature*, **234**, 463; 1971).

But whether the core formed during, or later than, accretion, there has been little suggestion so far that the mixture of iron and silicates from which the Earth accreted was anything but homogeneous; and it is this assumption of homogeneity which effectively defines what is now recognized as the conventional view of core formation. In this connexion the work of Elssasser (*Earth Science and Meteorites*, North-Holland, Amsterdam; 1963) may be regarded as representative.

In considering the early history of the Earth, Elssasser

started with an Earth which accreted cold and in which the material was uniformly distributed. The principal feature of such a model is that the melting point curve of the silicates rises much more steeply with depth than the actual temperature, which implies an appreciable rise in the viscosity of the silicates with depth. As the Earth is later heated by radioactive decay, the outer layers are the first to become soft enough to allow iron to move towards the centre. At greater depths, however, the sinking of the iron is slowed down by the increased viscosity, the iron forms a coherent layer which is gravitationally unstable, and the large drops which result fall rapidly to the centre forming a core. Elssasser's estimate of the time taken to form a core slightly smaller than the present one was about 10^8 years. Another, equally well known, model beginning with a homogeneous Earth was that of Birch (*J. Geophys. Res.*, **70**, 6217; 1965).

With Orowan (*Nature*, **222**, 867; 1969), however, a new idea emerged (albeit within the framework of a model which was perhaps less in keeping with mainstream thinking); namely, that the Earth may have accreted inhomogeneously right from the start. Orowan's point was that, even at low temperatures, iron is plastic-ductile as long as its carbon content does not vastly exceed that of meteorites. As a result, colliding metal particles may be expected to cohere because they can absorb kinetic energy by plastic deformation and can thus combine by cold or hot welding. Silicates, on the other hand, being brittle, break up on collision except at near melting point temperatures. The idea is then that the Earth's accretion began with metallic particles. Once sufficiently large, the growing Earth would then collect non-metallic particles by embedding them in ductile material and later by gravitational attraction. In other words, according to this view, the Earth formed with a metal core already partially differentiated, core formation and Earth accretion were thus simultaneous, and later core formation by differentiation was unnecessary.

The same year, Turekian and Clark (*Earth Planet. Sci. Lett.*, **6**, 346; 1969) also proposed an inhomogeneous model, but based on rather different principles. Their idea was that as the primitive solar nebula cooled, elements and compounds would condense in the order of increasing vapour pressure, an order defined by Larimer (*Geochim. Cosmochim. Acta*, **31**, 1215; 1967) as iron and nickel, magnesium and iron silicates, alkali silicates, metals such as Ag, Ga and Cu, iron sulphide, and metals such as Hg, Tl, Pb, In and Bi. In general terms such an order agrees with the stratification in the Earth usually attributed to differentiation. Thus, according to this model, condensed iron-nickel would first form the core which, as in Orowan's model, would become the nucleus for the deposition of silicate mantle.

There is little doubt that such inhomogeneous models need to be tested, if only because, as Ringwood (*Geochim. Cosmochim. Acta*, **30**, 41; 1966) pointed out some years ago, there are a number of difficulties with the conventional model. On the other hand, as Anderson and Hanks point out in this issue of *Nature*, the Turekian-Clark model has also hitherto been stuck with a problem—namely, that there is apparently not enough energy available to melt the outer core either during or after accretion. By eliminating this problem, Anderson and Hanks have now made the idea of initial inhomogeneity that much more attractive.—P. J. S.

A Chemical Curiosity

It is always interesting to find chemical curiosities and it is often in the course of kinetic studies that these turn up. Examples occur of concurrent or consecutive reactions which demonstrate, because of their relative rates or efficiencies, the build-up and decay of intermediate species. This is particularly attractive when an obvious colour change simplifies the observation and enables the observer to appreciate visually a new "art form".

A recent addition to the gallery is a reaction discussed by Field and Noyes on page 390 of this issue of *Nature*. This involves the reaction of bromate ion on malonic acid catalysed by cerium ions. Depending on the conditions of experiment, oscillations in the cerous/ceric ratio can occur either as a function of time or space and, as might be expected, this is accomplished by a series of interconnected reactions. The authors of the letter promise a subsequent discussion of the implications of this type of chemical sequence which may even provide an alternative to the familiar egg timer.—From a Correspondent.

X-RAY ASTRONOMY

Uhuru Dominates Madrid Meeting

from a Correspondent

THE IAU/COSPAR symposium on X-ray and γ -ray astronomy, held in Madrid on May 11–13, was in many ways historic. It took place only a month before the tenth anniversary of the discovery of the first cosmic X-ray source, Scorpius X-1, and was also the first international gathering to review the wealth of remarkable new X-ray observations from the Uhuru satellite, launched in December 1970.

The atmosphere of the meeting was notably different from that in Rome three years ago, when exciting new results were reported, but X-ray sources were still in the main essentially described only in terms of speculation. In contrast, at the Madrid symposium, attended, significantly, by leaders from all the related branches of optical, ultraviolet, radio and theoretical astronomy, several clear facts as to the nature of these powerful objects were generally accepted.

Dr H. Tananbaum (American Science and Engineering) discussed the Uhuru results on the eighty or so galactic sources, many of which exhibit remarkable short-term variability. Four have already been shown rather conclusively to belong to binary star systems, and other such identifications seem likely. The strong, irregularly pulsating source Cygnus X-1 was associated several months ago with a ninth magnitude supergiant B0 star on the basis of an apparent agreement between intensity changes in the 20–50 keV flux and the 5.6 day spectroscopic binary nature of the B0 star. Although no 5.6 day modulation of the lower energy (2–6 keV) X-ray flux has been seen by Uhuru, the coincidence in March–April last year of a major change in the overall X-ray intensity—falling by a factor of five or so—with the emergence of a variable radio source which lies within 1 arc s of the B0 star, seems to have now confirmed this binary system identification. Typically, from the dynamics of this binary system, it seems probable that the compact and optically unseen X-ray companion is greater than 3 solar masses and—according to current theory—will thus be a “black hole”.

A second source in Vela, GX263+3, has been found by Uhuru to lie within a few arc min of the sixth magnitude spectroscopic binary and may be similar to Cyg X-1. The weaker X-ray signals have so far not revealed short-term pulsations. The binary nature of two other galactic X-ray sources, Cen X-3 and Her X-1, has been established from the X-ray observations alone; the X-ray signals are

regularly eclipsed every 2.09 and 1.75 days, respectively. No acceptable optical or radio counterpart to either of these sources has yet been reported, though active searches of the relevant sky areas are in hand. An improved location of the Her X-1 source was reported (by Dr G. Clark of Massachusetts Institute of Technology from his OSO-7 data), lying within 0.15° (1σ) of RA=16 h 56.7 m and $\delta=35^\circ 35'$. These two sources show the remarkable property of regular and deep modulation in their X-ray intensity, with periods of 4.82 s in the case of Cen X-3 and 1.25 s for Her X-1.

It may well be that most galactic X-ray sources are in binary systems and this would help to explain the high X-ray luminosities (10^{36} – 10^{38} ergs s^{-1}). Dr J. Ostriker (Princeton University) and Drs M. Rees and J. Pringle (Institute of Theoretical Astronomy, Cambridge) were generally agreed in their discussions of source models that the X-rays resulted from accretion of gas from a giant or supergiant star on to its nearby, compact companion. Where the mass of the compact star is less than a critical value of $\sim 2 M_\odot$, the Cambridge model predicts the X-rays to arise chiefly from the surface of the star. If this star has a strong dipole magnetic field the largely ionized gas will be directed onto the magnetic polar regions, giving two “hot spots” on the stellar surface. A rotating neutron star, with its axes of rotation and magnetic field suitably inclined, was proposed to account in this way for the periodically varying sources Cen X-3 and Her X-1. If, for such as Cyg X-1, however, the compact object is a black hole then, of course, the observed X-rays would emerge only from the accreting disk of gas itself and short term regular variability would not be expected.

Dr E. Kellogg (American Science and Engineering) reviewed the observations of extragalactic sources by Uhuru. Based on their high latitude, these number about forty, of which fifteen or so have been provisionally identified. They range in luminosity from the nearby spiral galaxy in Andromeda (M31), with $L_X \sim 2 \times 10^{39}$ ergs s^{-1} , to the nearest QSO (3C 273), with $L_X \sim 10^{46}$ ergs s^{-1} . Powerful X-radiation is observed from several rich clusters of galaxies and in several of the nearer cases—in Virgo, Perseus and Coma, for example—the source is observed to be extended by several hundred kiloparsecs. Both Dr Kellogg and Dr G. Setti (Laboratorio di Astrofisica, Frascati) pointed out that the

number and intensity of the extragalactic sources already detected by Uhuru make it now more likely that the quasi-isotropic X-ray background is merely the integrated flux from such sources, with no major contribution being required from either a diffuse source, such as inverse Compton scattering of electrons on the universal microwave radiation, or from a strong evolutionary effect.

The nature of the X-ray production in the extended cluster sources remains unknown and both thermal bremsstrahlung and inverse Compton theories were discussed. Dr G. Burbidge (University of California at San Diego) probably carried most of the audience with him in arguing for the second model on the grounds that although very little evidence exists for any large mass of multi-million degree gas in these clusters, the presence of relativistic electrons within the observed X-ray emission regions is, in several of the sources listed, already demonstrated by the observation of similarly extended synchrotron radio emission. As Dr Burbidge pointed out, provided the magnetic field in the cluster does not exceed a microGauss, typically the observed X-ray flux will arise inevitably by electron interactions with the radio, infrared or microwave background photons. Though the spatial resolution of Uhuru is limited to objects greater than some 15 arc min, evidence for several highly compact extragalactic sources was presented, in terms of observed spectral attenuation, which must surely be intrinsic to the source. Such was the case for the Seyfert NGC 4151, the QSO 3C 273 and the strong and nearby radio galaxy Cen A.

Though Uhuru dominated the meeting, the continuing importance of rocket experiments was demonstrated in important results from new experiments outside the range of Uhuru's capability. Dr R. Angel (Columbia University, New York) reported a further attempt to observe the elusive iron line emission from Sco X-1 in a recent Aerobee rocket flight. Again no line was seen, pushing the (1σ) upper limit of the Leicester group down a further factor of seven to ~ 1 eV, for the equivalent widths of the resonance, intercombination and forbidden lines of helium-like Fe XXV. If Sco X-1 is also a binary accretion system—as seems probable, though no specific evidence of a binary nature yet exists—the X-ray emission may arise from an extremely compact region in which electron scattering and large velocity mass motion will very effectively destroy narrow line features. Examination of the detailed shape of the X-ray continuum may be more productive.

Rocket experiments searching the

sky in the technically difficult region below 1 keV have produced interesting results on both the quasi-isotropic background radiation and on inherently cool or "soft" X-ray sources. An increasing number of intense soft X-ray sources, associated with old supernova remnants, including Cygnus Loop, Vela X and Pup A, contrast with the notable absence of any new supernova remnants in the Uhuru catalogue of 2-6 keV sources in a review of this topic by Dr K. Pounds (University of Leicester).

Perhaps the best evidence yet for line features (OVII and OVIII?) was reported in the Cygnus Loop spectrum between 0.5 and 0.7 keV from a Cal-Tech rocket experiment, making use of 'Teflon' and oxygen filters. The indicated mono-energetic features were of the expected strength for a thermal X-ray source at a temperature of 3-4 million degrees, in line with the current view that soft X-rays probably arise in the older supernova remnants from the interstellar gas, heated by the expanding "blast-wave". Dr H. Friedman (Naval Research Laboratory) reported some of the most impressive data yet on the X-ray background below 1 keV. Galactic latitude scans in two ~0.15 and 0.25 keV energy bands are best fitted by a two component source model, consisting of the extrapolated (extragalactic) background spectrum observed at higher energies and suitably attenuated by absorption in the galaxy, together with a population of low energy galactic sources which contribute most of the flux at low latitudes. From the observed latitude distribution the scale height of these (as yet unresolved) sources was deduced to be some five times the neutral H scale height or ~500 pc.

γ -Ray astronomy was relegated to the last hour of the final day, which was unfortunate because intriguing new balloon observations by several groups brought evidence—albeit somewhat conflicting—of the first galactic γ -ray sources in the 20-100 MeV energy range. If even a fraction of the exciting γ -ray results are confirmed there is little doubt that this infant branch of astronomy will be able to hold its own much better against its now well-established spectral neighbour at the next symposium in three years time.

FISHERIES

Salmon-Trout Hybrids

from our Marine Vertebrate Correspondent
HYBRIDIZATION between various members of the salmon family has been recorded in the scientific literature for a very long time, but it was not until the intense interest taken in improving salmonid fisheries during the past cen-

tury that anything more than casual observations were made. With the establishment of trout hatcheries, especially that at Howietown, Stirlingshire, in the 1870s hybrids were produced experimentally between salmon and trout, and other species, with a view to producing fish more suited to cultivation. Similar experimental crossings of these two species have been produced in recent work in Ireland. First generation hybrids between salmon and trout are thus well known from artificial crossings but have been rarely found in the wild.

A recent study (in *J. Fish Biol.*, 4, 233; 1972) by R. H. Payne, A. R. Child, and A. Forrest of the Salmon and Freshwater Fisheries Laboratory, Weymouth, has attempted to assess the degree of natural hybridization in British waters. The two species are closely related and externally similar in their migratory stages so that blood samples were used to distinguish the parent species and their hybrids. The fish were supplied by commercial salmon fishermen in estuaries and in coastal waters and were thus a sample of the migratory population of salmonids. The blood of salmon and trout and their hybrids contains single serum esterases, but that of the salmon has greater electrophoretic mobility when subjected to electrophoresis in gels of alkaline pH. It is thus possible to demonstrate by this method differences between the two species and also to detect any natural hybrids.

Payne *et al.* studied blood samples from more than four thousand fishes which on external examination were apparently salmon. Seventeen (nearly 0.4 per cent) proved to be natural hybrids between salmon and trout. It is thus apparent that hybrids are rather more common in nature than had been appreciated. During the summer of 1970 four such hybrids, obtained from the Amble, Northumberland, fishery, weighed 1.8, 2.2, 2.8 and 3.8 kg. The authors note that three of these fish would have been commercially acceptable as "grilse" and the heaviest as "salmon" (grilse being commercially defined as salmon of less than 3.6 kg), a situation of some interest in view of the United Kingdom regulations regarding correct labelling of food fish.

The figures produced by Payne *et al.* show, however, that the level of introgression is generally low in British waters, except for the north-east coast. Judged on the number of hybrids found in the Northumberland fishery, and that of the River Esk, Angus (0.9 per cent and 0.7 per cent of samples of 537 and 1,160 respectively), introgression in this area is relatively frequent. As Payne *et al.* point out, however, it is possible that elsewhere introgression may be as frequent but

the hybrids might have the general appearance of sea trout and would thus not have been sampled as putative salmon. On the other hand, the higher level of introgression in north-eastern areas might be explained by the generally shorter lengths of north-eastern rivers, with a reduced number of spawning areas and trout and salmon may thus be brought together on the redds.

Payne *et al.* conclude by suggesting that in rivers with large trout populations and a small salmon run the fertilization of salmon eggs by male trout may be an important contributory factor to the extinction of salmon. This interesting suggestion deserves further consideration and study, especially in areas where salmon appear to be becoming scarce.

RIBOSOMES

Binding Sites in Sight

from our Molecular Biology Correspondent
NOTWITHSTANDING the diverting conjuring tricks that have been performed with ribosomes — incomparably the most spectacular of which is to pull functioning ribosomes out of a hat containing the fifty-odd proteins and three RNAs—almost nothing is still known about the manner in which a protein recognizes its particular slot on the RNA and the nature of the interactions that anchor it there. The isolation and characterization of the primary protein binding sites on the ribosomal RNA are the most desirable objectives now on the horizon, and the indications are that they may fairly soon be achieved.

It seems to be established that among the twenty proteins of the 30S subunit of *Escherichia coli* there are six which bind specifically and strongly to the RNA in the first step of the assembly process. The most forthright approach to the isolation of protein-specific sites on the RNA is to digest the complexes formed by these proteins with a nuclease, and isolate such parts of the RNA as may be protected by the bound protein. A promising start was reported not long ago by Schaup *et al.* (*Mol. Gen. Genet.*, 114, 1; 1972), who digested the 1:1 complex of 16S RNA and the protein S4 with T_1 ribonuclease, and found that about 30 per cent of the RNA was preserved in an apparently essentially homogeneous ribonucleoprotein fragment. Digestion and fingerprinting of the RNA allowed only a tentative identification of some of the oligonucleotides with sequence tracts from near the 5' end of the 16S chain. An interesting feature, however, is that the protected RNA is not an unbroken chain: when analysed by gel electrophoresis it turned out to con-

tain several fragments, all of which apparently were able to reassociate with the protein. The ability of so small a protein molecule to protect so vast a length of RNA is extraordinary and unexplained.

Now Zimmerman *et al.* (*Proc. US Nat. Acad. Sci.*, **69**, 1282; 1972) have varied this approach and extended it to the other primary binding proteins, and have gone some way towards localizing the six binding sites on the 16S RNA. They have prepared nuclease fragments of the RNA and tested them for ability to bind the proteins. T₁ RNA generates initially two large fragments of 12S and 8S, which comprise the greater part of the whole chain. With further digestion the 12S piece gives place to 10S and 4S fragments. Pancreatic ribonuclease, on the other hand, produces an 11S fragment, which in turn generates two smaller segments of 9S and 4S. Five of the six proteins bind to the 12S fragment, whereas one (S13) binds to the 8S. Nucleotide mapping shows that the 12S piece is essentially the 5' half of the 16S RNA, and the 8S adjoins it on the 3' side. The 4S fragment, which has 135 nucleotides, contains a site for only one of the proteins (S15). The S4 protein of Schaup *et al.* is the only one to bind to the pancreatic 9S segment, which comes from the 5' end of the 12S and therefore of the original 16S RNA.

The precise location of the fragments within the 16S chain is limited by the incompleteness of the sequence data so far available. The conclusion is, however, that five of the six primary binding sites are clustered rather closely together in one half of the chain. Moreover, a large part of the 4S RNA, which binds the protein S15, has been sequenced, and also partial sequence information for the 9S fragment, that binds S4, is presented. As Schaup *et al.* found, this fragment consists of several smaller pieces, which separate under denaturing conditions. In both cases there seems to be considerable scope for the formation of hairpin loops, with considerable base-pairing, but the precise relation of this to the RNA-protein interaction must await the isolation of smaller binding fragments—a project which Zimmerman *et al.* assure readers is in progress.

At the next, higher, level of ribosome assembly, protein-protein interactions come into play, and a good deal of effort is now being deployed on attempts to establish which proteins interact with which. A number of reports have appeared of the isolation of large fragments of the ribosome that contain some proteins and not others, and so allow the possible range of protein-protein contacts to be narrowed down. Most encouragingly

perhaps, Schendel *et al.* (*ibid.*, 544) were able, by hewing the 30S subunit into three pieces with nuclease, and identifying the proteins distributed between them, to relate the interactions which are compatible with this distribution to those dictated by Nomura's assembly maps. That is to say, those proteins, the incorporation of which into the 30S ribosome is contingent on the prior presence of the primary binding proteins on the RNA, are also present in the same nucleolytic subfragment as the latter.

This suggests that the assembly maps reflect direct physical interaction of the proteins which they link, rather than a merely conformation-directing role for the primary binding proteins. Bickle *et al.* (*ibid.*, 1327) have found that the action of a bifunctional reagent on 30S subunits leads apparently to the pairwise association of some of the proteins, but the information that emerges is insufficient to allow comparisons with the assembly maps. The interaction of the more readily dissociable proteins has also been studied, and Randall-Hazelbauer and Kurland (*Mol. Gen. Genet.*, **115**, 234; 1972) have found that the binding of tRNA to ribosomes is enhanced by augmentation of three proteins, S2, S3 and S14 (S1 being already known to promote messenger binding). These components may therefore well constitute

the A-site of the 30S ribosome.

The first step in identifying the interaction region on the 23S RNA for the 5S minor RNA component has been taken by Gray and Monier (*Biochimie*, **54**, 41; 1972). Earlier work from the same laboratory showed that a small group of large subunit proteins was required for the formation of a complex containing 5S and 23S RNA. Four proteins have in fact been identified as necessary and sufficient. Gray and Monier now find that the same trick is possible with a fragment of the 23S RNA, comprising about 60 per cent of the whole, and lying at the 3' end. Attempts will no doubt be made to repeat the experiment with smaller pieces.

IMMUNE RESPONSE

Genetic Control

from a Correspondent

A CONFERENCE on the genetic control of immune responsiveness: its relationship to disease susceptibility at Brook Lodge, Michigan, on May 8–10 showed how rapid developments in this field have greatly clarified certain issues but have left others obscure.

Studies with recombinant mice during the past two years carried out by Dr D. C. Schressler (Ann Arbor) have confirmed that there are two

SV40 Induces Nuclear Acidic Protein Synthesis

THE small DNA tumour viruses—polyoma virus and simian virus 40—share the property of inducing non-dividing cells which they infect to initiate a round of DNA synthesis; if the cells are non-permissive and survive, they subsequently mitose.

This triggering of DNA replication by polyoma virus and SV40 some 12 hours after infection involves all the cellular DNA, mitochondrial as well as nuclear, and in the nucleus it is accompanied by the induction of the synthesis of histone proteins required for the daughter chromosomes. But the chromosomes of mammalian cells contain considerable proportions of acidic proteins in addition to the basic histones. Is the synthesis of this class of nuclear proteins also induced after infection by polyoma virus or SV40?

The results of experiments which Rovera, Baserga and Defendi report in next Wednesday's *Nature New Biology* (June 21) indicate that in both permissive monkey CV1 cells and non-permissive secondary Chinese hamster fibroblasts synthesis of nuclear acidic proteins is indeed induced by SV40 infection. That may be entirely as expected, but what is interesting is that the induction occurs within 3 hours of infection,

well before the synthesis of DNA and histones is induced.

Using incorporation of ³H-leucine into acid insoluble material as an index of protein synthesis, Rovera *et al.* measured the synthesis of total cytoplasmic protein and of acidic nuclear proteins in CV1 cells and Chinese hamster cells 3 hours after infection or mock infection. At the multiplicities of infection they used, essentially all the cells were infected. In both infected permissive and non-permissive cells, while the rate of incorporation of ³H-leucine into cytoplasmic proteins decreases, the rate of synthesis of acidic nuclear proteins increases.

Precisely how, within 3 hours of infection, SV40 achieves this differential stimulation of the synthesis of host cell proteins is puzzling, but as Rovera *et al.* point out, by 3 hours after infection at least some SV40 particles have been uncoated and so the synthesis of viral proteins, including the trigger molecule, may have occurred. They also comment that the similarities between the pattern of synthesis of acidic nuclear proteins in cells stimulated to divide by SV40 or by serum are sufficient reasonably to suggest that both stimuli act through a common pathway.

genes controlling major histocompatibility antigens, separated by a short distance in linkage group IX on chromosome 17. One of these genes codes for the H-2^k product and the other for the H-2^d product; in addition to "private" specificities defined by specifically reacting antisera, the H-2 gene products share certain "public" specificities defined by cross-reacting antisera. As previously suggested for the human HL-A genes, it is likely that the two H-2 genes arose by duplication of a common precursor gene with subsequent mutation giving rise to private specificities. Separating the two loci for the K and D regions of H-2 are genes *Ss* controlling serum α -globulins and a group of *Ir* genes controlling immune responses to synthetic polypeptides and many other antigens, in the order *K*, *Ir*, *Ss*, *D*.

In several mammals certain *Ir* genes are closely associated with major histocompatibility genes, and much evidence has been accumulated by Dr H. McDevitt (Stanford School of Medicine) and others showing that these *Ir* genes exert their effects on thymus-dependent (T) lymphocytes. In some cases these genes also seem to affect reactions of B lymphocytes directly, but the evidence on this point is less compelling.

Marked differences in immune responses to other antigens are, however, associated with genetic control of the type of immunoglobulin synthesized by B cells, quantitative differences in antibody formation, allotypes and idiotypes (the specific determinants of individual immunoglobulin molecules produced by clones of cells) all being related. This has been shown by, for example, Drs R. Krowther (New York), A. Nisonoff (University of Illinois) and M. Cohn (San Diego). Still other immune response genes are not obviously associated with major histocompatibility types or allotypes. This information, together with genetic and chemical observations on independent control of constant and variable regions of immunoglobulins, has greatly increased understanding of the genetic control of immune responsiveness in general.

The antigen-binding receptor at the surface of B lymphocytes is universally accepted to be an immunoglobulin, but the nature of the T cell receptor for antigen remains elusive. Some groups of research workers, including Dr N. L. Warner (Melbourne), have presented evidence for the presence of immunoglobulin light chains and μ chains at the surface of T lymphocytes, but most investigators have been unable to find immunoglobulins related to the membranes of T cells, or inhibition of T cell reactions by antisera against immunoglobulins. One view is that

T cells have a non-immunoglobulin antigen-binding mechanism perhaps evolved from a primitive and widespread system of intercellular recognition. The relationships of the antigen-recognition system in T cells, major histocompatibility antigens and linked *Ir* gene products are still obscure, and it seems likely that detailed chemistry will be required to resolve this problem.

Genetic differences in susceptibility to disease may be manifested primarily in the reactions of immunocompetent cells or at other levels. An example which was discussed in depth by Dr F. Lilly (New York) was the interaction of several genetically-controlled factors in determining the resistance or susceptibility of mice to virus leukemogenesis. One of these factors is associated with H-2 type, and may be attributable to *Ir* genes. Relative differences in susceptibility of mice to lymphocytic choriomeningitis are also associated with H-2 type. But major genetic factors determine the ability of all cells from animals of a particular genotype to support virus replication, so that reactions of immunocompetent cells are not primarily involved in these cases. Several associations of human major histocompatibility antigens with particular diseases have come to light. These are difficult to interpret, as was emphasized by Professor W. F. Bodmer (University of Oxford) although their potential interest in eventually helping to reveal the genetic factors controlling

immune responses in man is clear.

This conference was the last of a projected series of five at Brook Lodge organized and sponsored by the US National Institute of Allergy and Infectious Diseases. A new cycle of these immunology conferences, with European support, will begin in Italy in June 1973.

TRANSLATION

Frameshift Mutations

from our Cell Biology Correspondent

THE existence and properties of frameshift mutations, resulting from the deletion or insertion of a base from a gene, proved that the codons of the genetic code are triplets of bases. Once a frameshift mutation is introduced into a gene (for example, the insertion of an additional base) the reading frame is shifted so that all codons distal to the mutation are read out of phase unless, of course, a second and compensatory frameshift mutation (in this case, a deletion of a base) occurs to restore the phase and reading frame, or unless the particular bacterial strain also carries a frameshift suppressor mutation.

The existence of external frameshift suppressor mutations, analogous to ochre and amber suppressor mutations, was first noted by Riyasaty and Atkins in 1968, who hinted that altered transfer RNAs might be involved. Subsequently Yournon and Tanemura (1970)

Rocks from the Rockall Plateau

ROCKS scooped from the seabed of Rockall Bank are described in next Monday's issue of *Nature Physical Science* (June 19). They were obtained simply by hauling a dredge across the seabed and the collection includes many specimens which can be recognized as glacial erratics. But among the material are fragments which look as if they may have been broken off outcrops and may therefore give some indication of the composition of the Rockall Plateau itself. Three different types of rock are represented in this class and are described by E. J. W. Jones (University College, London), J. G. Mitchell (University of Newcastle), F. Shido (State University of New York at Albany) and J. D. Phillips (Woods Hole Oceanographic Institution).

The Rockall Plateau lies beneath the North Atlantic between Ireland and Iceland and is believed to be a piece of the jigsaw puzzle that was broken up when the North Atlantic was formed and North America moved away from Western Europe. The Rockall Plateau is thought to have

gone with Greenland when Greenland was broken away from Europe in the Mesozoic, but later (during the early Tertiary) the plateau was also split from Greenland and became left behind as an isolated continental fragment submerged beneath the ocean, except for the tiny island of Rockall itself.

The three types of rock which have been recognized in the dredge haul are described as alkali olivine basalt, aegirine-riebeckite granite porphyry, and aegirine-riebeckite granite. Potassium-argon dating of samples of each rock type gives ages of about 54 million years (with the exception of the basalt which had an anomalously low age) which seem to be in accord with the beginning of the rifting which separated the Rockall Plateau from Greenland.

This is the first occasion that dredged rock samples from the Rockall Plateau have been dated, and the result is an indication of the igneous activity on the plateau presumably associated with the tensions occurring when the plateau was split from Greenland.

and Riddle and Roth (1970) pursued this idea and the second group isolated several strains of *Salmonella typhimurium* carrying such external suppressors. And in the current issue of the *Journal of Molecular Biology* (66, 483 and 494; 1972) Riddle and Roth report, first, the genetic mapping of these frameshift suppressor mutations and, second, their association with altered tRNA species.

Riddle and Roth's collection of suppressors map at six distinct and widely separated loci defining six suppressor genes (*sufA-F*) and the location of the *sufD* gene on the *S. typhimurium* chromosome corresponds to the location of a glycine tRNA gene on the *Escherichia coli* chromosome. The genetic maps of these two species are very similar and so from the genetic data alone it would not be surprising if the *sufD* gene proved somehow to be related to a glycine tRNA gene. The fact that four of the suppressor mutations, *sufA*, B, D and E, are dominant to the corresponding wild type genes when these are introduced on an F' episome is also, of course, consonant with the idea that these genes may specify altered tRNAs.

The crucial test of such an idea is, however, the isolation from the mutant strains of tRNAs capable of frameshift suppression *in vitro*. Riddle and Roth have gone some way towards this goal by showing that in strains carrying either the *sufA* or *sufB* genes two proline tRNAs have changed mobilities on benzoylated DEAE-cellulose columns, while the *sufD* gene is associated with an altered glycine tRNA and the *sufF* gene is associated with an increased heterogeneity of glycine tRNAs.

Riddle and Roth have not managed so far to associate the *sufC* and *sufE* genes with altered tRNAs, but that does not, of course, rule out the idea that these suppressors act by way of tRNA. In short, there seems little doubt that at least some external frameshift suppressor mutations cause changes in tRNAs and they may well be located in the structural genes of those molecules. It will, of course, be most interesting to learn the base sequences of the altered tRNA, for that information may give clues to the mechanism of suppression, which, it is widely supposed, involves tRNAs reading quadruplets instead of triplets of bases in regions of an RNA where one base is repeated several times and thereby restoring the reading frame.

Everybody working with frameshift suppressors has envisaged suppression by tRNAs because of the amber and ochre suppressor precedents. It is not surprising therefore that Gorini and his colleagues should have searched, with success, for mutations of ribo-

somal proteins which also lead to the suppression of frameshift mutations. Atkins, Elseviers and Gorini, for example, have just reported (*Proc. US Nat. Acad. Sci.*, 69, 1192; 1972) that the leakiness of sixteen different frameshift mutations in the lac operon of *E. coli* is controlled by the ribosome. In cells with wild type ribosomes some β -galactosidase is made in spite of the frameshift mutations. But when the *strA* mutation, which alters the P10 protein of the 30S ribosomal subunit and also restricts errors and ambiguity of translation, is introduced the amount of β -galactosidase made, the leakiness in other words, is cut to barely a fifth of its previous level. Moreover, when the *ram* mutation is also introduced (the *ram* mutation alters the P4a ribosomal protein and antagonizes the restriction of the *strA* mutation) the amount of β -galactosidase made, at least in some cases, is restored to the levels detectable in cells with wild type ribosomes.

These data indicate that the structure of the ribosome has a role in the suppression of frameshift mutations presumably by promoting or restricting the frequency of translation of quadruplets of bases by wild type tRNAs. If this idea is correct one might predict that cells carrying frameshift suppressor mutations affecting tRNAs as well as the *ram* mutation affecting the ribosomes would suppress frameshift mutations with very high efficiencies.

APPLIED ECOLOGY

Computerized Ecosystem

from a Correspondent

RESEARCH into the complex inter-relationships within ecological systems has received considerable impetus from the development of analogue computer techniques. The cycling of minerals within ecosystems has proved a particularly suitable field for the application of systems analysis and the consequent generation of predictive models. In the current issue of the *Journal of Applied Ecology* (9, 25; 1972) P. F. May, A. R. Till and M. J. Cumming (CSIRO, Australia) describe the application of such techniques to the study of the movement of sulphur in sheep-grazed pastures and its final accumulation in wool.

Data for the model have been collected during the past eight years and chiefly involve the use of sulphur-35 as a radioactive tracer. Sulphur was initially applied to an experimental grassland in New South Wales in 1964 as ³⁵S-gypsum and its movement was followed during the course of 760 days. The rates of incorporation of the tracer were measured in the soil, in plant tissue, in the ingested herbage (measured by fistulation), in the wool and in the excreta of the sheep. These rates, in May *et al.*'s opinion, represent the major pools within the system and are easily measurable. Other subsidiary pools, such as the soil organic matter and the

Different Scrapie Agents Compete

IN next Wednesday's *Nature New Biology* (June 21) Dickinson, Fraser, Meikle and Outram report a series of experiments which leave no room to doubt that different strains of scrapie agent simultaneously infecting the same mouse interfere competitively with each other's replication. Dickinson and his colleagues have used for their experiments VM mice as hosts and the 22A and 22C strains of scrapie agent. In VM mice 22C strain has a much longer incubation time than has 22A and the pattern of brain lesions caused by these two strains differs such that in doubly infected VM mice 22A and 22C lesions can be distinguished.

Dickinson *et al.* set out to discover whether these two strains of scrapie agent act synergistically or competitively when both are inoculated in the brain or peritoneum of a host. Because the 22C strain from C57Bl mice replicates so much more slowly than does the 22A strain from VM mice, it was necessary to inoculate the VM host with the 22C strain first and then challenge afterwards with the 22A strain.

From such experiments Dickinson *et*

al. find that, if the 22C intracerebral injection precedes by some 5-9 weeks the 22A injection, the incubation period of the 22A-induced brain lesions is increased by at least 30 days. An injection of 22C agent one week before an injection of 22A agent does not, by contrast, prolong the latent period.

From these and other observations Dickinson *et al.* reach several tentative conclusions. First, it seems likely that the slowly replicating 22C agent may compete with the 22A agent and slow its replication by blocking a significant proportion of putative sites at which the agents can replicate. Second, the slow replication of the 22C strain and the failure to observe competition against the 22A strain when the interval between the two injections is short suggests that at least in VM mice the 22C strain may have to be somehow modified or processed before it can bind to a significant number of the putative replication sites. Third, there is no evidence of any synergism between these two strains and the competition that is observed is unlikely to involve an orthodox immune response.

sulphur pool immediately available to plants, are more difficult to measure.

May *et al.* conclude that the system approximates to a closed one with very little loss of sulphur over the experimental period. The maintenance of high tracer activity in the wool suggests that sulphur is continually cycled but rates of isotope dilution indicate that only a small proportion of the total soil sulphur was available to plants.

The authors report how they used an analogue computer to simulate this soil-grass-sheep system; the cycling process is described in terms of a set of simultaneous differential equations, the coefficients of which represent transport rates between pools within the system. Some of these rates were unknown and were deduced by electronic adjustment until the output corresponded with the experimental data. Best fit was obtained when it was assumed that there were two plant pools which had differential absorption rates for sulphur and which were selectively eaten by lambs and ewes respectively.

From the model it has become evident that about 40 per cent of the total sulphur within the system is not involved in the cycle and that 90 per cent of the cycling sulphur must be held in organic material within the soil where it is not immediately available to plants. The rate at which such sulphur is released in an available form would appear to limit its incorporation into plant and animal tissue.

This type of model not only provides an efficient description of the pool size and transport rates of materials in an ecosystem but also allows the prediction of the outcome of selected perturbations. Such predictions can be tested empirically and the model thus improved. Predictive models of this type will prove increasingly valuable in situations where a particular pool is to be harvested, where pollution effects are to be studied or where a plan for habitat conservation is required.

PHOTOBIOLOGY

Excited States

from a Correspondent

THE detection and relevance of excited states in photosynthesis and vision was the subject of a symposium held at the Royal Institution, London, on May 30. Jointly organized by the British Photobiology Society and the Photochemistry Discussion Group of the Royal Institution, and sponsored by the European Science Exchange Programme of the Royal Society, the conference provided a well illustrated picture of some physical techniques being applied today in the study of photobiological systems.

Dr M. A. West (Royal Institution) summarized some recent advances in the

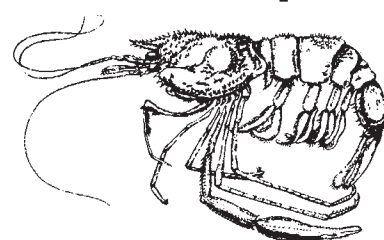
detection of electronically excited states. He suggested that solid state and wave-length tunable dye lasers have become increasingly important as excitation sources because of their advantages of selective excitation, enhanced time resolution and increased sensitivity. Properties of biological systems following pulsed laser excitation include transient linear dichroism in retinal rods and excited states have been observed using ESR spectral decay. The use of fluorescence to study excited singlet states was discussed in terms of the highly sensitive technique of single photon counting. Dr West noted the elegant adaptation of this technique by Brand and co-workers who have measured time resolved changes in fluorescence emission spectra.

The role of accessory pigments in protecting the chloroplast against photodynamic action was discussed by Dr P. Mathis (Centre d'Etudes Nucléaires, Saclay) who presented flash photolysis results on the triplet states and radical cations of various carotenoids. The triplet state of all trans β -carotene, produced in various environments (chloroplasts, solvents, micelles) by triplet-triplet energy transfer from chlorophyll, is relatively insensitive to changes in temperature or nature of the solvent, but triplet decay in the presence of oxygen is accelerated. Inasmuch as Dr Mathis believes that carotenoid triplets have energies of 17 kcal/mole, and are therefore important in deactivating reactive singlet oxygen, the quenching by oxygen of these triplets has been interpreted as a purely physical, non-energy transfer process. In a related series of investigations, Dr F. Kaufman (Royal Institution) has studied triplet state deactivation by molecular oxygen and nitric oxide.

Dr W. Junge (Max Volmer Institute, Technical University, Berlin) discussed the repetitive flash photolysis technique to study the small, very rapid changes of excited state absorptions in photosynthetic systems. The intrinsic electrochromic absorption changes of chloroplast bulk pigments indicate the light induced membrane potential. In recent experiments Dr Junge has found that the dye cresol red, added to chloroplasts in known concentrations, indicates pH changes in the outer phase of the functional vesicles of photosynthesis. The addition of methyl viologen or ferricyanide, two substances which interact with the electron transport chain, resulted in absorption changes which could be readily correlated with the predicted net translocation of protons. In comparing the results from both the intrinsic and extrinsic probes, Dr Junge proposed a mechanistic model which related the light activated proton movements with the electric potential gen-

CRUSTACEA

Southern Shrimps



Stenopus hispidus, from a new guide, *Shrimps and Prawns of Southern Africa*, by B. Kensley of the South African Museum.

erated across the functional photosynthetic membrane.

Professor W. Kreutz (University of Freiburg) has also used pH indicators to detect light induced pH changes in the outer phase of visual rod outer segments. He has coupled the fast photochemical reaction techniques with low angle X-ray scattering to gain insight into the structural and functional relationships of the visual process. Professor Kreutz said that his X-ray studies show the importance of structural protein and type of phospholipid in determining the structure of membranes. Furthermore, he has found evidence for isothermal phase transitions in phospholipids, induced and controlled by pH, where the latter was affected by CO₂ concentration in solution.

In contrast to these studies by microscopic approach, Dr W. A. Hagins (National Institutes of Health) described his electrophysiological measurements on retinal photoreceptors which led to the proposal of a two-stage excitatory process for rhodopsin. The electrical behaviour of the receptor layer of the isolated rat retina was investigated with micropipette electrodes inserted by direct visual observation using infrared microscopy. It was found that the light activated excitation process produced a transitory decrease in sodium permeability of the cell membrane. Calcium was shown to mimic the effect of light with regard to sodium permeability and Dr Hagins proposed a model in which light initiates a flow of calcium ions that acts to reduce the sodium permeability of the plasma membrane.

The conference provided the participants with an opportunity to learn of the wide ranging subjects (photophysics to physiology) which are currently being used in photobiology. One message which they may have taken away with them concerned the application of spectral probes where size prevents study by more direct microscopic methods. These microscopic probes can easily be used to indicate changes in physically observable parameters.

The Visual System and "Neuronal Specificity"

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To explain how neurones make the correct connexions during development and growth, Sperry put forward his hypothesis of neuronal specificity, in which neurones are recognized by individual chemical labels. The basis for this specificity is still unclear; but recent evidence suggests that it may be more appropriate to think in terms of "systems matching" than of the matching of individual cells.

SOME thirty years ago R. W. Sperry put forward a hypothesis to account for the orderly way in which connexions are formed between various classes of nerve cells during embryonic development¹⁻³. Sperry's hypothesis, which is now widely accepted, was originally formulated in relation to the connexions between the eye and the brain in the amphibian visual system and was based on the concept of neuronal specificity. Retinal ganglion cells display differential behaviour in their modes of connexion. Nasal retinal ganglion cells selectively link with caudal optic tectum, temporal retinal ganglion cells with rostral tectum, ventral ganglion cells with medial tectum and dorsal ganglion cells with lateral tectum. After consideration and rejection of extrinsic factors such as mechanical guidance or functional adaptation, Sperry was led to argue that the differential behaviour of optic axons reflected intrinsic differences between the retinal ganglion cells.

On this view retinal differentiation extended to include differentiation of the morphologically homogeneous ganglion cells, one from another, according to their position in the retinal field. This further differentiation conferred on the retinal ganglion cell a high degree of "specificity", in the sense of uniqueness; and it was this "specificity" which underlay the selectivity with which the ganglion cells would form synaptic connexions. This process of specification, involving processes of differentiation in an embryonic field, was believed to occur at an early stage of development and certainly before the onset of visual function.

Sperry conceived of the specificity as essentially cytochemical in nature and also postulated a comparable and matching cytodifferentiation among the population of developing tectal cells. Optic axons growing out from the retinal ganglion cells were presumed to carry with them the "specificity" characteristics of the parent cells. When the growing axons reached the tectum specific chemical affinities, existing as a result of the parallel specification processes in retina and tectum, enabled each optic axon to connect selectively and exclusively with its appropriate opposite number in the tectal cell population.

Evidence from Lower Vertebrates

The general popularity of Sperry's model rests not only on its elegance and its accord with known principles of

development, but also on two critical pieces of experimental support. The first is the demonstration that the pattern of retinotectal connexions is indeed determined at an early stage of development, before the onset of visual function. The developmental time at which the ganglion cells acquire their unique properties (of eventual axon termination) has been determined by rotating the eye through 180° at various stages before the formation of retinotectal connexions and studying, later, the resulting pattern of connexions⁴⁻⁶. It turns out that the critical time is the early tail-bud stage of the embryo: rotation before this results later in normal visual connexions; rotation later than this produces eventually a comparably rotated field projection to the optic tectum, indicating that the pattern of retinal connexions with the tectum, or some mechanism controlling this, had been determined before the rotation of the eye. This tail-bud stage has, therefore, come to be called the period of "specification" of the retinal ganglion cells.

The second important piece of experimental support for the notion of specific interneuronal chemoaffinities came from experiments in which size disparities were produced between the retina and the tectum. Before we can accept the view that a given nerve fibre will connect selectively and only with a given predesignated target, we need evidence that the fibre will select its "proper" target even if given the opportunity to connect with alternative sites. Attardi and Sperry⁷ obtained such evidence. They performed a variety of partial retinal ablations, together with section of the optic nerve, in adult goldfish. The regenerating fibres from the remaining retina formed connexions solely with the appropriate tectal sites, in some cases having crossed empty tectal areas to reach their own synaptic zones. This type of result, achieved by histological methods, furnished considerable support for the specific chemoaffinity hypothesis. Comparable findings were obtained in the embryonic chick visual system⁸ and Jacobson and Gaze⁹ described similar results from electrophysiological mapping in the adult goldfish. With a wealth of evidence supporting it, the view that the embryonic location of a retinal ganglion cell rigidly determines the location of its axonal termination has come to be widely accepted.

The first indication that this elegant hypothesis might be misleadingly simple came from work on surgically constructed "compound eyes" in *Xenopus*^{10,11}. A compound eye was formed by uniting two nasal or two temporal half-eye cups at developmental stage 32 of *Xenopus*; that is, at a stage after retinal ganglion cell "specification". Electrophysiological mapping of the fibre projection from such an eye to its contralateral optic tectum after metamorphosis might have been expected to show that the fibres from a double-nasal eye restricted their projection to the caudal half of the tectum, while those from a double-temporal eye occupied only the rostral half of the tectum. This was not found. The fibres from each half-retina of the compound eye (either double-nasal or double-temporal) spread their connexions over the entire rostrocaudal extent of the tectum. It thus seemed that one and the same part of the tectum was capable of forming ordered connexions with either nasal or temporal retina. This suggested that the neural relationship between retinal and tectal cells was far less rigid than that implied in

the hypothesis of neuronal specificity. Alternative interpretations of this "compound eye" result were recently examined in an experimental situation where the optic chiasma was uncrossed and the normal and compound eyes were each induced to innervate directly their own ipsilateral tectum¹². The results obtained were interpreted as indicating that the connexions formed by a given retinal ganglion cell depend not only on the retinal situation of that ganglion cell and the tectal situation of a tectal cell, but also on the extent of the retinal fibre complement projecting to the tectum and the extent of the tectum available. We have called this type of mechanism "systems-matching" to emphasize its difference from the selective and exclusive cell-to-cell specificity implicit in the chemoaffinity hypothesis.

None of the work in this field, including our own, has yet succeeded in distinguishing unequivocally between the various interpretations that we are discussing. Evidence suggesting a form of systems-matching has, however, been obtained in the adult goldfish retinotectal system. Gaze and Sharma¹³ found that after removal of the caudal half of the tectum the entire visual field of one eye could map, in order, onto the remaining rostral half-tectum. Yoon¹⁴, in an elegant series of experiments, showed that this type of field-compression occurred not only along the rostrocaudal tectal axis but also along the mediolateral tectal axis (in this latter respect these results contradict the earlier findings of Jacobson and Gaze⁹). Yoon interpreted his results as indicating a respecification of the tectal elements following surgical interference with the tectum; and although this is a feasible interpretation of his results, it does raise the question of whether it is useful to talk of "specificity" in this context. We are dealing here with adult goldfish; and if each time we get a different result we say that the specificity has changed, it is difficult to see what is added to our understanding of the situation by this usage.

The original formulation of the hypothesis of neuronal specificity was based on the apparent invariability of retinotectal connexions. We now know, however, that these connexions are not invariant. They can alter, but they do so in an ordered fashion. Recent work on the development of the retinotectal projection in *Xenopus* tadpoles¹⁶ suggests that the tectal projection of a given retinal ganglion cell progressively alters as the animal grows and, as a corollary, the retinal input to a particularly tectal cell progressively alters during larval life. The main characteristics of the retinotopic ordering of the projection are preserved during growth, yet there appears to be a continuous variation in specific intercellular relationships.

The data just discussed entail at least a modification of the specific chemoaffinity theory. In view of this we must now ask just what was "specified" during the critical period of retinal ganglion cell specification. It has in the past been assumed that at this stage the central connexions of the ganglion cells become fully determined⁵. This is not so. First, as we have just pointed out, the embryonic location of the ganglion cell does not, of itself, completely determine the tectal connexions that the cell will form. These connexions are not constant during larval life; and even in adult life the connexions depend (in goldfish at least) on the extent of other retinal fibres present and on the amount of tectum available for innervation. Second, at stage 31 (*Xenopus*, tail-bud) only a small fraction of the immediate ganglion cell precursors are yet present. Most of the ganglion cell precursors undergo their final DNA synthesis after stage 31¹⁷. The majority of ganglion cells thus do not appear until later, and in some cases much later, than the critical period hitherto called the period in which these cells were held to become "specified".

Clearly, therefore, the events of stages 29–31 do not directly "specify" the ganglion cells of the adult retina, most of which are not present at this time. The results of the eye-rotation experiments discussed earlier show that the

developing retina has some property stamped on it at stages 29–31, and that this property is impressed on the retina with reference to some entity outside the developing eye-cup. We should, perhaps, return to the terminology of Stone^{6,18,19}, who talked of the "polarization" of the retina in the early optic cup stage. It appears that what is determined during stages 29–31 is the polarity of the developmental axes of the retina, with respect to the connectivity pattern of the future ganglion cells. The suggestion of Sperry³ and the work of Székely⁴ and Jacobson⁵ indicate that there must be at least two such axes.

The mode of action of these developmental axes is unknown. A view akin to that of Sperry might be that ganglion cells which appear after the polarization of the retinal axes are then exposed to and acquire the appropriate positional information (Wolpert^{20,21}) according to their position with respect to the coordinate field defined by the two axes. The retinal ganglion cell may interpret this information by, for example, the graded synthesis of specific macromolecules and in this manner become cytochemically different from its fellows. On this view the concept of neuronal specificity would survive. It is the case that retinal ganglion cells behave differently one from another; and this governing the nature of the interconnexions between two differential behaviour could be, as Sperry originally proposed^{1–3}, directly related to the existence of cytochemical differences between the cells. In this case, however, the rules such "specified" neuronal arrays would have to be different from those originally envisaged by Sperry. The nature of the rules is being sought at present; the effect of the rules is that, in *Xenopus* and goldfish at least, interconnecting structures tend to match up as systems, rather than as a series of discrete, independent subunits.

Connexions in the Mammalian Visual System

We now briefly consider the extent to which concepts deriving from studies on the development of lower vertebrate visual connexions may apply to mammalian visual systems. Mammals possess the phylogenetically older retinotectal (collicular) system, but have elaborated diencephalic and telencephalic projections into what is generally assumed to be the dominant retino-geniculo-striate system.

There is evidence that the broad pattern of retinotopic connexions in the cat visual system is established before the onset of normal visual function^{22,23}. It seems that function has a role to play in the maintenance of some synaptic connexions^{23,24} and may even have a part in the organization of some of the finer points of receptive field properties^{25–28}; but the general retinotopic order of visual connexions to the cortex precedes visual function. We may note here that there is a comparable controversy at present about the role of visual function in the maintenance and/or establishment of visual connexions in the amphibian intertectal system^{29–31}. Here, however, we are considering only those mechanisms which are prefunctional in the sense that they are not dependent on visual function.

Given the prefunctional nature of the mechanisms involved in the formation of these selective connexions in mammals, we may ask whether they operate as a system-to-system matching or whether they work on the basis of specific cell-to-cell affinities. As in the lower vertebrates, these alternatives might be distinguished by observing the effects of a relative size disparity between the innervating and the innervated structures. Deliberate surgical intervention to create size disparities has not yet been done in mammals. Recent studies on Siamese cats, however, indicate that in these animals such a disparity occurs naturally^{32–34}. It seems that a number of retinal fibres are misrouted at the optic chiasma; fibres from a variable amount of retina temporal to the *area centralis*, instead of remaining on the ipsilateral side of the

brain, cross over to the contralateral side. The dorsal lateral geniculate nucleus and superior colliculus on each side are, therefore, presented with a larger quota of retinal fibres than normal from the contralateral eye and a reduced input from the ipsilateral retina. In the absence of information to the contrary, and for the sake of our present discussion, we shall assume that this is the only significant abnormality in the visual system of the Siamese cat.

The way in which the anomalous input is handled has been studied at the level of the geniculate by Guillery and Kaas³³, Hubel and Wiesel³⁴, and Kalil *et al.*³⁵; at the level of the cortex by Hubel and Wiesel³⁴; and at the level of the superior colliculus by Berman and Cynader³⁶. The results obtained in these three situations do not lead to a uniform conclusion. Broadly, the mapping of the colliculus and the striate cortex has yielded results compatible with a systems-matching type of scheme. The additional input from the temporal retina of the contralateral eye projects, in order, in front of (or medial to, in the case of the cortex) that from the normal nasal retinal input; the latter being progressively displaced. Hubel and Wiesel commented that their observations on the cortex indicated the lack of a "detailed cell-to-cell specificity of geniculocortical connexions, but rather a tendency to topographic order and continuity"³⁴.

Observations on the geniculate, on the other hand, have given results more in keeping with a strict cell-to-cell affinity. The normal nasal input from the contralateral eye projects normally to lamina A. The lateral part of lamina A₁, which in the cat normally receives innervation from the peripheral temporal retina of the ipsilateral eye, does so also in the Siamese cat. The medial part of lamina A₁ would have received input from the more central temporal retina of the ipsilateral eye, had these fibres not aberrantly crossed at the optic chiasma, but instead it is occupied by the aberrant fibres from the central temporal retina of the contralateral eye. The extra quota of fibres from the contralateral eye is thus slotted into that part of the LGN left "vacant" by the non-arrival of some of the fibres from the ipsilateral eye (Fig. 1).

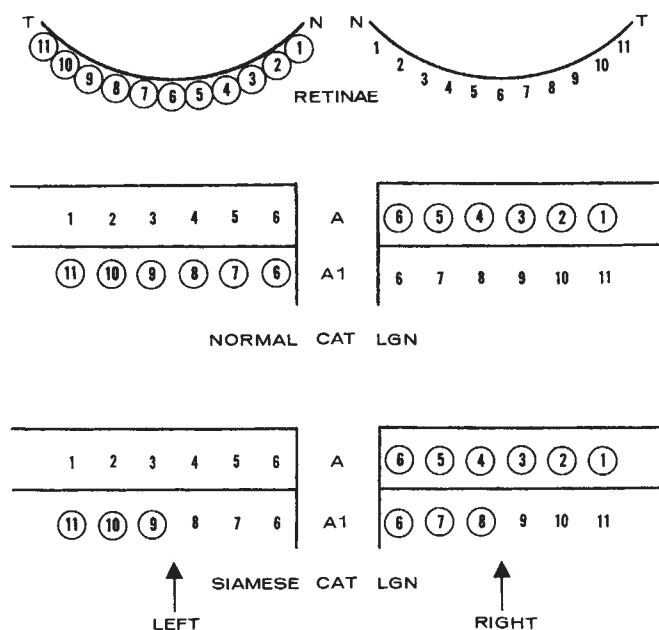


Fig. 1 Simplified diagrammatic representation of the retinal projection to laminae A and A₁ in the lateral geniculate nucleus of normal and Siamese cats, based on the findings of Guillery and Kaas³³ and Hubel and Wiesel³⁴. In Siamese cats fibres which normally project to the ipsilateral side of the brain ((6), (7), (8), and 6, 7, 8) decussate at the optic chiasma and project to the medial part of lamina A₁ of the contralateral geniculate.

The retinotopic arrangement of the aberrant axons from the contralateral eye is such that the fibres terminate at their "normal" sites in the geniculate; they just happen to be in the wrong geniculate (Fig. 1). Both Guillery and Kaas³³ and Hubel and Wiesel³⁴ interpreted this as indicating that the retinal ganglion cells were properly specified for their geniculate terminations but improperly specified for their chiasmatic crossing. These results and interpretations are quite different from those that might be predicted on a systems-matching basis, in which we could have expected that the aberrant fibres from the contralateral eye should squeeze into the medial aspect of lamina A, displacing laterally the normal input; while the reduced input from the ipsilateral side might be expected to spread out to occupy the entire extent of lamina A₁.

It therefore seems that in response to the arrival of an extra group of retinal fibres, the mechanisms ordering retinotectal (collicular) connexions behave quite differently from those ordering retinogeniculate connexions. We seem led to the conclusion that different mechanisms operate to generate the pattern of connexions in the phylogenetically younger retinogeniculate system from those operating in the older retinotectal system. Superficial consideration of the cortical map in Siamese cats would, however, lead to the conclusion that in the phylogenetically youngest system—the geniculocortical—we have again returned to the older mechanism of systems-matching.

This would be puzzling enough if true. In fact, if the retinogeniculate projection in Siamese cats is as Guillery and Kaas³³ and Hubel and Wiesel³⁴ state, and if the cortical map is as Hubel and Wiesel describe, then the geniculocortical connexions are neither normal nor do they seem to us to display the type of topographic order that Hubel and Wiesel mention, and which we call systems-matching (Fig. 2). Hubel and Wiesel's conclusion that the geniculate axons "arrive at the cortex in a topographically ordered fashion and simply fill out the available space"³⁴ seems to do less than justice to the degree of abnormality outlined by their data.

It can be seen from Fig. 2 that the axons of the geniculate cells of lamina A₁ are not projecting to the cortex in a continuous topographic order. It is also clear that the geniculate cells (6), (7) and (8) are not behaving like geniculate cells normally situated at these sites. It is, in fact, not easy to conceive of a mechanism operating to produce the pattern of geniculocortical connexions illustrated in this figure.

We are thus left with the conclusion that the patterns of synaptic connexions in three visual neural systems in the same animal are determined by three different mechanisms: a systems-matching in the retinotectal pathway; a cell-to-cell specificity in the retinogeniculate pathway; and a bizarre, analysis-defying mechanism in the geniculocortical projection. This is obviously an unsatisfactory view to hold; and it seems to us that the data or interpretations leading to it should be re-examined. If the experimental findings are confirmed, then attention should be turned to the interpretations. For example, we might question the nature of the cells occupying the medial aspect of lamina A₁ in Siamese cats. To account for the manner in which the abnormal fibres from the contralateral temporal retina connect with medial A₁, it was assumed that the geniculate cells in that area were those normally occupying medial A₁. In that case we encounter the serious problem of accounting for the mode of connexion of these cells with the cortex, which is totally unlike that of normal medial A₁ cells, and is not the simple topographic order described by Hubel and Wiesel. If, on the other hand, we propose that the cells occupying medial A₁ are not the normal cells, then while we may be able to avoid the problems of geniculocortical connexions, we are left with the difficulty of accounting for the retinal projection to the geniculate.

It is possible to construct explanations of the data on the basis that the cells occupying medial A₁ in the Siamese cat are in fact displaced lamina A cells into which the contralateral retina has "systems-matched". Such explanations are

survey of recent results in the study of neural development leads us to think that it is time for us to reassess our verbal coinage. Perhaps the most obvious outcome of all this recent work is the demonstration that our present concepts

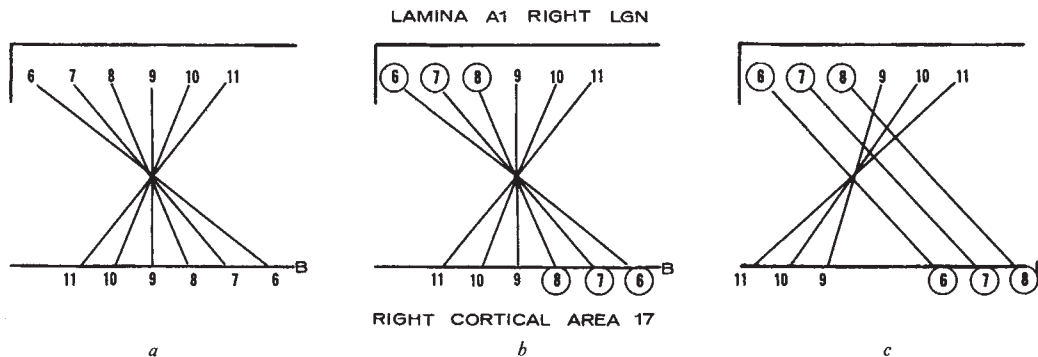


Fig. 2 *a*, Diagram of geniculocortical connexions from lamina A₁ of the geniculate to area 17 of the visual cortex in the normal cat. B represents the boundary between cortical area 17 medially and area 18 laterally. *b*, The projection to cortical area 17 from lamina A₁ of the Siamese cat, on the basis of either normal or "topographically ordered" geniculocortical connexions. It may be seen that this does not give the dominant cortical distribution described by Hubel and Wiesel³⁴, which is shown in diagram *c*. *c*, The pattern of geniculocortical connexions from lamina A₁ in Siamese cats, given the findings of Hubel and Wiesel³⁴.

themselves, however, associated with some fairly formidable difficulties of interpretation and terminology. Formerly it was feasible to attempt to account for the development of mammalian visual connexions on the basis of a modified neuronal specificity hypothesis—modified to deal with the non-eye-equivalence of the partially-decussating mammalian visual system¹⁵. The recent work on Siamese cats suggests strongly that workers in this field in mammals are now beginning to encounter some of the fundamental problems which have for some time been evident in the work on submammalian forms—problems associated with understanding what we may mean by saying that a cell is "specified", when our only measure of cellular uniqueness is the distribution of its connexions.

At this stage in the development of the hypothesis of neuronal specificity it may be useful to question even the basic postulates on which the hypothesis rests. It must be acknowledged that there is, in fact, no evidence that requires the view that the formation of synapses at specific sites is due to any form of neuronal chemospecificity. The attractive argument that because two cells behave differently they must, therefore, be intrinsically (cytochemically) different is compelling only if all possible extrinsic influences have been eliminated, which is not the case. Differential behaviour of two ganglion cells need not, therefore, imply cytochemical differentiation; the two cells could be cytochemically similar but exposed to, and influenced by, different extrinsic factors. The nature of such factors, even if they exist, is unknown; but their effects would have to be spatially distributed in a fashion determined by the developmental polarization of the retina and the tectum. Specific connexions do not necessarily imply "specified" neurones.

There is much confusion at the present time in the study of the interconnexions between neurones in the vertebrate brain. This is partly due to the inherent difficulty of the subject—there are too many neurones—and partly to the vague and ill-defined terminology that has traditionally been used to discuss neural connexions. Terms such as order, randomness and specificity have been commonly used; and it becomes more obvious with each paper published that each author is using a private language and the terms that he uses may mean one thing to him and quite another to someone else. These comments, of course, are equally true of us. Our brief, necessarily selective, and therefore incomplete

are insufficiently precise. Further advance in this field depends on sharper definition of our ideas so that their adequacy can be more clearly tested in the experimental situation.

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Origin of the Low Energy Diffuse Cosmic X-Ray Flux

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While only the gross features of the low energy diffuse flux have been observed, it seems that a galactic component of diffuse soft X-rays is required. Forces of this flux should be distributed about the galactic plane with a scale height similar to that of the hydrogen.

IN the photon energy range above 2 keV the diffuse cosmic X-ray flux closely approximates a differential spectrum of the form $kE^{-1.5}$. In the energy range 0.1 to 2.0 keV, there is considerable disagreement about the nature of the diffuse flux. But most observations¹⁻⁶ seem to suggest that the intensity below 1 keV is greater than that which would result from an extrapolation of the $E^{-1.5}$ power law, that the intensity at high galactic latitudes is greater than at low latitudes and that the intensity of the radiation in the galactic plane is greater than can be supplied easily by the extrapolated power law spectrum after passage through the interstellar medium.

The variation of flux with galactic latitude is complex, but experiments which have scanned a considerable range of latitudes^{2,4,5} indicate that for $|b^{\text{II}}| \lesssim 30^\circ$ there is a correlation of low energy emission with hydrogen column density (N_{H}). At latitudes less than $|30^\circ|$, a correlation of soft X-ray flux with N_{H} is not seen.

The variation of the low energy diffuse X-ray flux with galactic latitude is determined by the interaction of the X-rays with the interstellar medium. Because the level of flux observed in the plane suggests the existence of a galactic component, studies of the latitude variation of the flux give information about the nature of both the galactic and extra-galactic components of the soft X-ray flux. Rees⁷ has suggested that the interaction of a galactic soft X-ray flux with the interstellar gas can lead to a maximum in intensity at low to intermediate galactic latitudes.

We assume that the number density of soft X-ray sources is given by $N_{\text{S}} = N_{\text{SO}} \exp(-Z/a)$, where Z is distance out of the galactic plane, and that the hydrogen density varies as $N_{\text{H}} = N_{\text{HO}} \exp(-Z/b)$. The hydrogen column density along a line of sight r at an angle θ to the galactic plane is given by $N_{\text{H}}(\infty) = N_{\text{HO}} b \csc \theta$. If individual sources have luminosity L at $E \sim 0.25$ keV and if σ is the photoelectric absorption

cross section of the interstellar medium at this energy⁸, then

$$\frac{dF}{d\omega} = A \int_0^\infty \exp(-ar) \exp(\beta e^{-\gamma r}) dr \quad (1)$$

where F is the 0.25 keV diffuse X-ray flux from a solid angle element $d\omega$, $\alpha = \sin \theta/a$, $\gamma = \sin \theta/b$, $\beta = N_{\text{HO}} b \sigma / \sin \theta$ and $A = (N_{\text{SO}} L/4\pi) \exp(-N_{\text{HO}} b \sigma / \sin \theta)$. Substituting $y = \exp(-ar)$ into equation (1), we obtain

$$\frac{dF}{d\omega} = \frac{A}{\alpha} \int_0^1 \exp(\beta y^\alpha) dy \quad (2)$$

where $\gamma/\alpha = a/b$, the ratio of the source distribution scale height to the hydrogen scale height.

At 0.25 keV, $\sigma = 4 \times 10^{-21} \text{ cm}^2$ (ref. 8) and, assuming $N_{\text{HO}} = 1 \text{ cm}^{-3}$, we have used equation (2) to obtain plots of soft X-ray flux against galactic latitude; the integral term is integrated numerically on a digital computer. But when the hydrogen distribution scale height b is compared with measured values of N_{H} above the plane⁹, the value of b does not remain constant with galactic latitude. This is partly because the hydrogen distribution about the galactic plane is probably better described by a Gaussian in Z^2 (ref. 10) but also because the interstellar medium is cloudy and the change of N_{H} with increasing latitude is by no means smooth⁹. Because of its convenience, we have chosen to use equation (2) to calculate the variation of flux with latitude and to vary the value of b for latitudes out of the galactic plane. To obtain the variation of b with latitude we have averaged Tolbert's column densities⁹ for the longitude range $l^{\text{II}} = 120^\circ$ to $l^{\text{II}} = 170^\circ$. Even after averaging, there are substantial fluctuations in N_{H} for latitudes around 40° , so we have drawn a smooth curve through points of N_{H} plotted against latitude. We have used the plot to obtain the fractional decrease in the value of b with respect to its value near the plane. If more certain X-ray data with better spatial resolution were available, this procedure could hardly be justified; but it seems permissible at present since only the gross features of the X-ray latitude variation have become apparent.

Using equation (2) we have plotted normalized soft X-ray flux ($dF/d\omega$) against galactic latitude (Fig. 1). The curves are consistent with the suggestion made by Rees⁷. For source scale heights equal to or greater than the hydrogen scale height, the flux shows a maximum near the galactic plane with

the latitude of the maximum increasing with source scale height. When the source scale height is greater than twice the value of the hydrogen scale height, however, there is a steep increase in flux from the galactic plane up to the maximum value at a latitude of 30° or greater. Similar behaviour is observed for all values of hydrogen scale height.

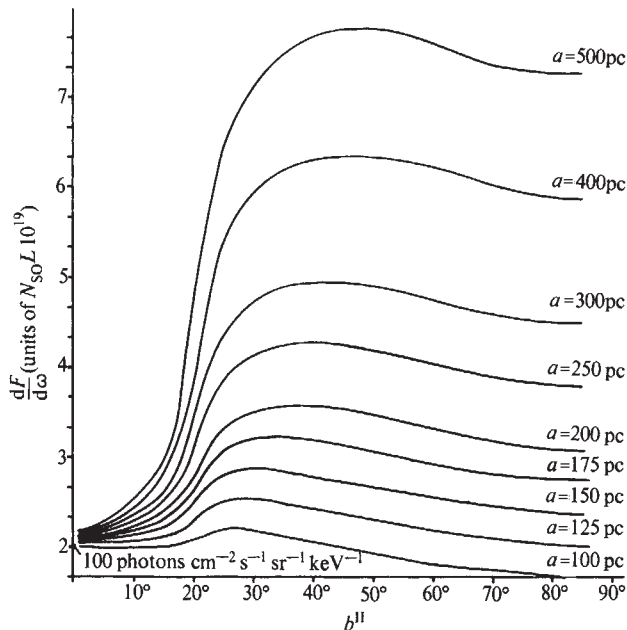


Fig. 1 Normalized X-ray flux. $b = 100$ pc at $b^{\text{II}} = 0^\circ$ for all curves; free parameter is source scale height a .

The experimental data now available present a somewhat confused picture. Pertinent data from four experiments are given in Table 1. In each of these cases a scan in galactic latitude was carried out and, as we have already pointed out, several investigators find a fair correlation between low energy diffuse X-ray flux and galactic latitude for latitudes above $b^{\text{II}} \approx 30^\circ$. It seems (Fig. 1) that if the observed pole to plane flux ratio of about 3.0 (see Table 1) were to be explained entirely on the basis of a galactic flux, then a source scale height of at least 400 pc would be required. This would result in the flux being essentially independent of galactic latitude above 30° , and would conflict with the available data. The galactic component of the flux can therefore only be supplied by a population of sources with a distribution scale height that is equal to or slightly greater than (up to about 1.5 times) that of the hydrogen. Such a population of objects leads to a flux that is either independent of latitude or slightly peaked at latitudes below 30° , in agreement with the observations. If the hydrogen scale height is about 100 pc, it is unlikely that the galactic population of flare stars, with a scale height of 350 pc, can give the observed dependence of flux on galactic latitude above 30° . This rules out the model of Cavallo and Horstman¹¹.

Because the permitted galactic source distributions lead to a soft X-ray flux which peaks at low galactic latitudes and does not increase with increasing latitude, the observed increase in flux at high latitudes must arise from an extragalactic or circumgalactic component. The experimental results^{4,5} suggest a soft X-ray flux in the plane of the Galaxy of about 100 photons $\text{cm}^{-2} \text{s}^{-1} \text{sr}^{-1} \text{keV}^{-1}$ at 0.25 keV. The value at the poles must therefore be around 300 photons $\text{cm}^{-2} \text{s}^{-1} \text{sr}^{-1} \text{keV}^{-1}$. We take $a = 150$ pc as the source distribution scale height; the

corresponding flux in the latitude range 0° to 20° must be around 100 photons $\text{cm}^{-2} \text{s}^{-1} \text{sr}^{-1} \text{keV}^{-1}$ to agree with the observations. It is clear from Fig. 1 that the galactic source component at high latitudes must then be about 120 photons $\text{cm}^{-2} \text{s}^{-1} \text{sr}^{-1} \text{keV}^{-1}$. The observed galactic polar flux is about 300 photons $\text{cm}^{-2} \text{s}^{-1} \text{sr}^{-1} \text{keV}^{-1}$ and therefore we require an additional flux of 180 photons $\text{cm}^{-2} \text{s}^{-1} \text{sr}^{-1} \text{keV}^{-1}$ at polar latitudes.

In the energy range 2 to 40 keV the diffuse X-ray component has a spectrum of the form²

$$\frac{dN}{dE} = 11E^{-1.5} \text{ photons cm}^{-2} \text{ s}^{-1} \text{ sr}^{-1} \text{ keV}^{-1} \quad (3)$$

which leads to a flux of 100 photons $\text{cm}^{-2} \text{s}^{-1} \text{sr}^{-1} \text{keV}^{-1}$ at 0.25 keV. The data of Tolbert⁹ show that $N_{\text{H}} \sim 10^{20}$ H atoms $(\text{cm}^{-2} \text{column})^{-1}$ in the polar direction. This means that an extrapolation of equation (3) to low energies will result in a flux of 70 photons $\text{cm}^{-2} \text{s}^{-1} \text{sr}^{-1} \text{keV}^{-1}$ near the Sun. Therefore the sum of the galactic component and the extrapolated extragalactic spectrum provides about 200 of the 300 photons $\text{cm}^{-2} \text{s}^{-1} \text{sr}^{-1} \text{keV}^{-1}$ that are observed at high latitudes. At $b^{\text{II}} = 30^\circ$, the extragalactic power law spectrum provides only 20% of the flux from the galactic component so it will not greatly influence the nature of the latitude variation below $b^{\text{II}} = 30^\circ$.

Table 1 Experimental Data on Low Energy Diffuse Component

Approximate limits of galactic scan "Plane"	"Pole" to "Plane" flux ratio	Ref.	Remarks
$l^{\text{II}} = 210^\circ$ $b^{\text{II}} = 0^\circ$	$l^{\text{II}} = 170^\circ$ $b^{\text{II}} = +60^\circ$	$\sim 2.5 \pm 30\%$	* Correlation with galactic hydrogen above $b^{\text{II}} = 30^\circ$. Peak at $b^{\text{II}} = 20^\circ$
$l^{\text{II}} = 215^\circ$ $b^{\text{II}} = 0^\circ$	$l^{\text{II}} = 236^\circ$ $b^{\text{II}} = -55^\circ$	$\sim 3.4 \pm 20\%$	2 Correlation with galactic hydrogen above $b^{\text{II}} = -35^\circ$. Little variation with b^{II} from 0° to -30°
$l^{\text{II}} \sim 80^\circ$ $b^{\text{II}} = 0^\circ$	$l^{\text{II}} \sim 80^\circ$ $b^{\text{II}} = -60^\circ$	$\sim 4.6 \pm 50\%$	5 Some correlation with galactic hydrogen above $b^{\text{II}} = -15^\circ$. Possible peak at $b^{\text{II}} = -5^\circ$
$l^{\text{II}} = 147^\circ$ $b^{\text{II}} = 0^\circ$	$l^{\text{II}} = 10^\circ$ $b^{\text{II}} = 60^\circ$	$\sim 2.8 \pm 30\%$	4 Some correlation with galactic hydrogen above $l^{\text{II}} = -20^\circ$. Little variation with b^{II} from 0° to -20°

The average pole to plane ratio is about 3:1.

* D. J. Yentis and colleagues, unpublished data.

The uncertainties in the experimental data are substantial, so the need for an additional extragalactic component of 100 photons $\text{cm}^{-2} \text{s}^{-1} \text{sr}^{-1} \text{keV}^{-1}$ at high latitudes is not yet demonstrated conclusively. But in view of the recent observation of the Small Magellanic Cloud by the Wisconsin group¹², any additional component is likely to be associated with our own Galaxy and will not be a universal phenomenon.

Mack¹³ has considered possible candidate sources of a galactic soft X-ray component. From energy considerations, he concluded that old supernova remnants, accretion on old neutron stars¹⁴ and hot plasma around magnetic white dwarfs¹⁵ are possible galactic soft X-ray sources. Here, we conclude that the scale height for such a population should be similar

to that of the hydrogen, so the first two models appear viable in that the X-ray production originates by an interaction with the gas.

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Role of Pollen-Wall Proteins as Recognition Substances in Interspecific Incompatibility in Poplars

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Proteins in pollen grain walls are essential for germination in poplars; they also affect the incompatibility systems on which pollen tube growth is dependent.

ONE reason for the failure of interspecific hybridization in flowering plants is that pollen from one species will not germinate on a foreign stigma, even when the second species appears to be closely related. This is why Michurin and his successors¹⁻³ in the USSR tried to overcome this obstacle to hybridization by mixing incompatible with compatible (mentor) pollen, in the hope that the latter would provide the necessary stimulus for germination and tube growth. Although the first attempts were not conspicuously successful, Stettler has more recently obtained hybrids between incompatible species of poplar by using mentor pollen killed by gamma radiation⁴. We have been able to repeat Stettler's experiments with other species of poplar⁵ and now demonstrate that the function of the killed compatible pollen is to provide what we have previously called "recognition substances"⁶⁻¹⁰. These constitute a large part of the protein

located in the inner cellulose layer of the pollen grain wall (intine)^{6-9,11-13}.

The proteins with enzymatic, antigenic and allergenic properties are in the intine or inner cellulosic layer of the pollen grain wall^{6-9,11-13}. They occur in strands, ribbons or leaflets encased in the polysaccharide matrix, and are readily released on moistening, when they diffuse out through the exine, particularly at the germination apertures. The enzymes released are acid hydrolases, which probably play a part in the emergence and early nutrition of the pollen tube, and in some species probably also in stigma penetration. The enzymatic proteins, however, constitute only a fraction of the total substances released. We have suggested that the major part is concerned in compatibility reactions⁶⁻¹⁰. We have applied the description "recognition substances" to these proteins, since we consider them to be a heterogeneous group, concerned with the control of pollen germination and tube growth in both inter- and intra-specific matings.

Experiments with both killed "recognition pollen" and extracts were carried out using *P. deltoides* as female parent and *P. alba* as male parent. Grafted scions were grown in protected conditions in a glasshouse⁵. The cross between *P. deltoides* and *P. alba* always failed to produce progeny in control pollinations, although the recognition pollen method⁵ has always resulted in successful hybridization in both directions. Large numbers of progeny can be produced (more

than 500 hybrids between *P. deltoides* and *P. alba* have been obtained) and all the progeny were hybrid⁵. When pollen of *P. alba* was mixed with inviable γ -irradiated pollen of *P. deltoides* and used for pollination, an average seed set of 5.0 seeds/capsule resulted, about 15% of that expected from the use of viable *P. deltoides* pollen (35.0 seeds per capsule) and the progeny were wholly hybrid. A comparable level of seed set was obtained when recognition pollen of *P. deltoides* killed with methanol was used (4.5 seeds per capsule), and of some 30% when the *P. deltoides* pollen had been killed by repeated freezing and thawing (11.0 seeds per capsule). This is obviously an excellent case for the test of the hypothesis that the wall-held proteins are the recognition factors concerned.

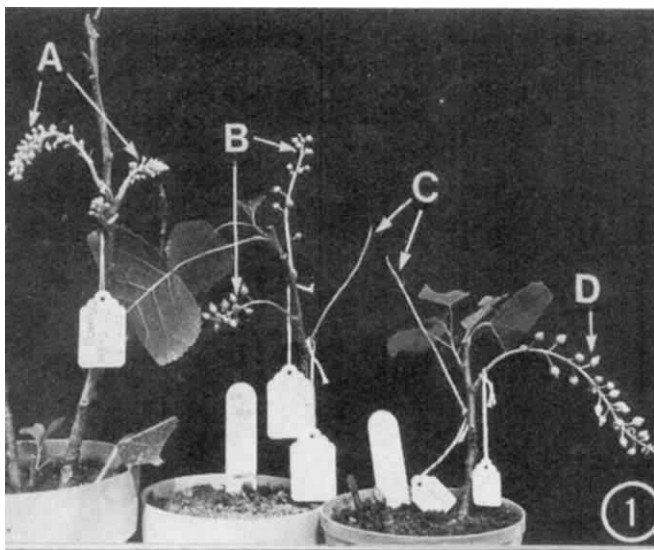


Fig. 1 Grafted branches of *P. deltoides* bearing female inflorescences. A, Appearance of inflorescences when stigmas are receptive. B, 3 weeks after pollination with incompatible *P. alba* pollen together with lyophilized saline extract of *P. deltoides* pollen added. The fruits have enlarged as in compatible mating (see D), and were subsequently shown to contain hybrid seed. C, 3 weeks after pollination with incompatible *P. alba* pollen without added extract. Fruits have abscised. D, 3 weeks after a compatible pollination showing developing fruits.

For the separation of the rapidly leachable proteins, dry pollen of *P. deltoides* that had been stored at -18°C was extracted in 1% saline at pH 7.5 for 2 h at 5°C with constant agitation. The extract was then dialysed against water for 15 h to remove the salt and other low-molecular-weight contaminants, including growth substances and co-factors. After dialysis, the extract was lyophilized. In several experiments, a yield of 26–28 mg of dry, fluffy proteinaceous material was obtained per 1 g of dry pollen. This material was used thoroughly mixed with viable *P. alba* pollen in approximately equal volumes.

The results of a typical experiment are shown in Fig. 1. In compatible control pollinations, the ovaries swelled, and seeds matured after about 8 weeks, while in pollinations using the viable but untreated pollen of *P. alba*, the ovaries all abscised. With pollen of *P. alba* bearing saline extracts of proteins derived from that of *P. deltoides*, a high proportion of ovaries swelled in the normal way. The average seed set per capsule was 2.7, less than that obtained with mixes using recognition pollen, but all progeny were hybrid, and the significance of the result is not in doubt. In recent

experiments, we have used conditions of extraction which precluded the loss of high-molecular-weight compounds from the pollen protoplasts, suggesting that the active substances were leached from the wall. Such extracts, after two precipitations with ammonium sulphate at 0.9 saturation^{14,15}, were equally successful in production of hybrid seeds.

The diversity of the pollen wall proteins of *P. deltoides* is demonstrated by immunodiffusion and immunoelectrophoretic studies. Antigens were prepared from short term saline leachates⁷, and antisera raised in rabbits. Using anti-*P. deltoides* serum, three precipitin lines were obtained by double diffusion in agar, two of the lines showing spur formation characteristic of partial immunological identity when tested against antigens of *P. alba*. By immunoelectrophoresis in agarose at pH 8.8, at least five antigens were detected. The intine localization of these antigens was confirmed by immunofluorescence methods^{7,8}. When slurries of mature pollen were freeze-sectioned, the antigens were localized as haloes around the grains; they had evidently diffused from their wall sites on moistening. When anthers containing mature pollen approximately 24 h before dehiscence were freeze-sectioned, however, precise localization of the antigens within the intine was obtained (Fig. 2).

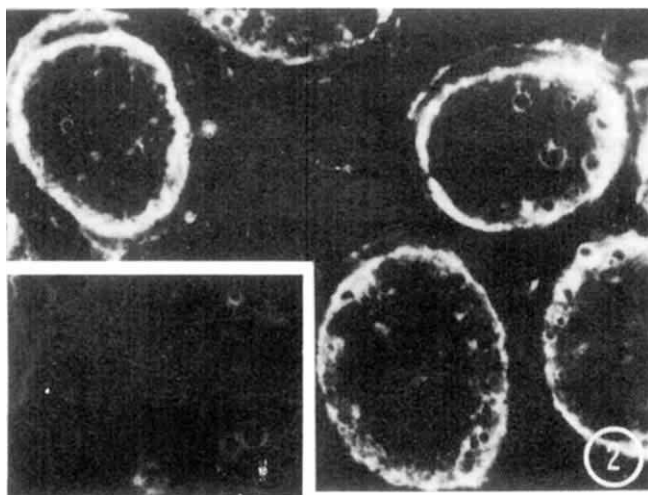


Fig. 2 Immunofluorescence localization of pollen wall antigens of *P. deltoides*. 2 μm frozen sections of mature anthers treated with specific anti-*P. deltoides* serum followed by anti-rabbit gamma globulin serum labelled with fluorescein isothiocyanate (FITC). Inset shows control treated with normal rabbit serum followed by FITC-labelled anti-rabbit gamma globulin serum. Most of the specific fluorescence is located in the inner intine layer of the pollen grain walls. Cytoplasmic fluorescence around starch grains is non-specific, being also present in the control ($\times 1,140$).

In work on other genera, the release of the antigenic proteins of the intine on to the surface of the stigma has been followed using immunofluorescence methods. In the grass *Phalaris tuberosa*, a rapid discharge of antigens before pollen germination was observed in both compatible and incompatible matings¹⁰. In *Ambrosia tenuifolia* (ragweed) and the related species, *Cosmos bipinnatus*, we have found that the antigens are lost on to the surfaces of the stigma cells in a similar way, and it is noteworthy that antigen E, known to be the most potent human allergen of ragweed pollen¹⁵, is among them. In the light of the present demonstration that proteins of pollen from *P. deltoides* can be used to disguise pollen of *P. alba* and make it acceptable to the stigmas of *P. deltoides*, it became of interest to trace the

behaviour of the wall-held antigens on the stigma in these species by the same methods¹⁰. Results were essentially as in the species of Gramineae and Compositae previously examined. In both compatible and incompatible matings, the antigens are rapidly released from the grains, spreading over the adjacent stigma surface within 10 min of pollination. After the emergence of the pollen tubes, fluorescing precipitins were particularly conspicuous over the surface of the tubes (Fig. 3). No reactions within the tissues of the stigma were observed using the immunofluorescence technique, and stigma homogenates failed to form precipitin lines when tested against the anti-*P. deltoides* serum by gel diffusion.

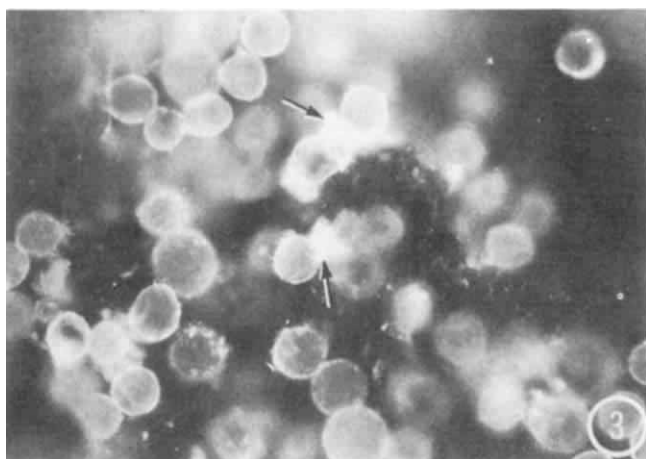


Fig. 3 Immunofluorescence localization of antigens diffusing from pollen grains of *P. alba* on a stigma of *P. deltoides*. Complete mount of stigma and grains placed in anti-*P. alba* serum 240 min after pollination. Fluorescing precipitins can be seen on the stigma surface adjacent to pollen grains and surrounding pollen tubes (arrow) in this incompatible mating. At this stage, no distinction in behaviour of antigens can be made between compatible and incompatible matings ($\times 285$).

Taken together, these results support the proposition that proteins held in the wall of the pollen grain are directly concerned in the control of pollen germination in the poplar species studied, and exclude the possibility that other pollen-borne factors are involved. The experiments described here concern barriers to pollen germination in interspecific crossing. In work on the self-incompatibility system of species of Compositae, we have obtained significant increases in seed set after selfing using the recognition pollen technique, which suggests that in sporophytically determined intra-specific incompatibility systems the wall-borne proteins may also be concerned. The nature of the reaction at the stigma surface—and indeed the identity of the factors with which the wall-borne proteins interact—remains obscure, although several mechanisms have been suggested^{16,17}. These new findings add an additional fact, namely that whatever the reactions between the pollen-borne proteins of incompatible pollen and materials at or in the stigma surface which prevent germination in the *P. deltoides* ♀ $\times$ *P. alba* ♂ cross, they must be such that they can at least be partly inhibited, neutralized or overwhelmed by the simultaneous presence of proteins from compatible pollen, since in these experiments no attempt was made to remove the wall proteins of the foreign pollen.

We have followed the events during the germination of self and foreign pollen on stigmas of *P. deltoides* using a decolorized aniline blue fluorescence method¹⁸. Both qualitative and quantitative differences in pollen germination, stigma penetration and pollen tube length characterize compatible and incompatible matings. When pollinated with *P. deltoides*, most grains germinated, the tubes penetrating and growing through the thaloid stigmatic tissue, polarized towards the style, many reaching it within 90 min after pollination. Using foreign *P. alba* pollen, only a small percentage of grains had germinated and produced short non-polarized tubes by this time. Between 7 and 20 h after pollination, however, some of these tubes became polarized, penetrated, and grew through the stigmatic tissue towards the style. No fertile embryos resulted from these matings in *in vivo* pollinations.

These studies of the kinetics of pollen tube growth support suggestions that self-recognition systems operate in incompatibility reactions in plants^{7,9,10,19,20}. In the case of poplars, the recognition is apparently at the supra-species level. For this reason, it would seem unlikely that these experiments shed direct light on the events of gametophytically determined self-incompatibility systems where the control is imposed at the infra-species level. Rapidly released proteins, probably derived from the intine, seem to be concerned in these^{21,22}, but the nature of the control—specific to each pollen grain—shows that there can hardly be any massive interaction between different grains, even when they are intimately mixed, as the *S* genotypes must certainly be on release from the anther. Such diversity of behaviour points to the multiplicity of mechanisms that may control compatibility reactions, pollen tube growth and fertilization.

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LETTERS TO NATURE

PHYSICAL SCIENCES

Low Frequency Radio Emission from Extensive Air Showers

THE observed radio emission from extensive air showers at frequencies between 30 and 100 MHz is in good agreement with theory¹. Both the typical field strength per unit bandwidth, $\mathcal{E}_\nu$, and the lateral distribution of the radiation about the shower axis can be given a quantitative interpretation. At lower frequencies the situation is much less satisfactory. Theory predicts that $\mathcal{E}_\nu$ should rise smoothly from zero at $\nu=0$ towards the observed values at 30 to 100 MHz, but the experimental values between 2 and 5 MHz are about 100 times larger²⁻⁵. The calculation presented here is intended to set a generous upper limit to $\mathcal{E}_\nu$, based on the least controversial elements of the theory. Because the claimed experimental values are greater even than this upper limit, I suggest that further checks are needed.

The basic formulae have been derived and discussed (ref. 6). They are reliable in that they are shown to lead to well established results, for example, concerning Čerenkov radiation. The first formula deals with short tracks, the second with long tracks.

If a charge e changes its angular bearing by $\delta\theta$ in a time $\ll 1/2\pi\nu$ as seen from some field point, then the field strength per unit bandwidth at the point of observation is

$$d\mathcal{E}_\nu = \frac{4\pi e}{c^2} \nu \delta\theta \text{ (gaussian units)} \\ = 2 \times 10^{-7} \nu \delta\theta \quad \mu\text{V m}^{-1} \text{ MHz}^{-1} \quad (\nu \text{ in MHz}) \quad (1)$$

For a charge moving in a straight line with velocity $v \approx c$ the field strength per unit bandwidth at a perpendicular distance r from the path is

$$\mathcal{E}_\nu = 4ev/c^2r \text{ (gaussian units)} \\ = 2 \times 10^{-5}/r \quad \mu\text{V m}^{-1} \text{ MHz}^{-1} \quad (r \text{ in metres}) \quad (2)$$

The formula $\mathcal{E}_\nu = 4ev/c^2r$ for a long straight track applies when the refractive index of the medium $\mu=1$. When $\mu>1$, the field strength becomes greater at high frequencies through the Čerenkov effect. At low frequencies the field strength is unchanged. The changeover from "low" to "high" occurs at a wavelength $r/10$ m, or frequency $3,000/r$ MHz (ref. 6). For the present discussion, with $r<100$ m, Čerenkov effects may therefore be ignored.

I consider an element of particle track dl in the shower at height H above the receiving antenna. If it is to give its maximum possible contribution to the total field, it must be oriented so that the angular displacement $\delta\theta$ in equation (1) is a maximum. This maximum value is dl/H . Suppose the maximum value of $\delta\theta$ is achieved for every element of track, and that the directions of the displacements are such that the contributions to $\mathcal{E}_\nu$ from positive and negative charges add. The total particle track length available in the height interval H to $H+dH$ is $N(H)dH$, where $N(H)$ is the number of shower particles at that height. The maximum contribution to

$\mathcal{E}_\nu$ is therefore

$$d\mathcal{E}_\nu = 2 \times 10^{-7} \nu N(H) \cdot dH/H \\ = 2 \times 10^{-7} \nu N(H) d \log_e H \quad \mu\text{V m}^{-1} \text{ MHz}^{-1}$$

I now integrate over the whole range of heights H , again making the assumption that all contribution to $\mathcal{E}_\nu$ reach the receiving antenna in phase and are coherent. Then as an absolute upper limit to the total field strength

$$\mathcal{E}_{\nu\text{max}} = 2 \times 10^{-7} \nu \int N(H) d \log_e H \quad \mu\text{V m}^{-1} \text{ MHz}^{-1}$$

Estimates of the magnitude of the integral depend on how $N(H)$ varies with H and on the appropriate limits of integration. Typical curves are given in ref. 1. The upper limit of integration is easily fixed at ~ 10 km because $N(H)$ is negligible at greater heights. In practice the lower limit cannot be less than 10–100 m because of the size of receiving antennae and the size of the air shower disk. The range of $\log H$ is thus ~ 5 or 6. Within this range $N(H)$ has a maximum value N_{max} near $H=5$ km and much smaller values at the extremes. A reasonable estimate is therefore

$$\int N(H) d \log_e H = 2 N_{\text{max}}$$

If the shower primary energy, $E_p = 2 \times 10^9 N_{\text{max}}$ eV, as is usually accepted, the upper limit to the field strength is

$$\mathcal{E}_{\nu\text{max}} = 2 \times 10^{-16} \nu E_p \quad \mu\text{V m}^{-1} \text{ MHz}^{-1} \\ (\nu \text{ in MHz, } E_p \text{ in eV})$$

Thus for $\nu=5$ MHz, $E_p=10^{17}$ eV, the maximum field strength is $100 \mu\text{V m}^{-1} \text{ MHz}^{-1}$. This value will not be approached in any real situation. I have supposed that the entire motion of the charged particles is transverse, with positive and negative particles moving in exactly antiparallel directions. All Coulomb scattering has been ignored, and by implication the forward motion of the shower is entrusted to neutral particles. No allowance has been made for the loss of coherence due to geometrical effects or the atmospheric refractive index: all contributions are assumed to be precisely in phase. The situation is a purely conceptual one, designed to make the most efficient radiating system possible from the available track length, subject only to the condition that the correct distribution of shower particle numbers with height is preserved.

The calculated value for $\mathcal{E}_{\nu\text{max}}$ is still less than the values of $\sim 1 \text{ mV m}^{-1} \text{ MHz}^{-1}$ that have been inferred from the experiments. The contradiction is complete.

The highly idealized model used to calculate $\mathcal{E}_{\nu\text{max}}$ supposes that the motion of the charged particles in the shower is entirely transverse. I now consider another model in which it is supposed that the charged particles move exactly parallel to the shower axis. I further assume that each charged particle track is of infinite length, so that the shower size does not change with height. The field from an individual track then depends on equation (2) above:

$$\mathcal{E}_\nu = K/r \quad \mu\text{V m}^{-1} \text{ MHz}^{-1} \text{ with } K = 2 \times 10^{-5} \quad (r \text{ in metres})$$

$\mathcal{E}_\nu$ is a vector; it lies in a plane perpendicular to the particle track, and is directed radially. The $(1/r)$ dependence leads

immediately to a two dimensional version of Gauss's theorem for the outward flux of $\mathcal{E}_v$ through a path that encloses the track. If $\mathcal{E}_v^\perp$ is the component of $\mathcal{E}_v$ perpendicular to the path then the line integral of $\mathcal{E}_v^\perp$ round the path must be $2\pi K$. I apply this theorem to a shower of N particles, taking as the path for the line integral a circle of radius R about the shower axis. The density of particles r m from the axis of a shower is given approximately by⁷

$$\Delta = N/500 r \text{ particles m}^{-2} (r < 40 \text{ m})$$

Some of these particles have positive charge, others negative charge. The effective number of charged tracks is $\varepsilon\Delta$, where ε is the so-called charge excess. ε is $\sim 10\%$ for shower particles of energy $E \sim 10$ MeV, and decreases with increasing E (roughly $\propto 1/E$)⁸. The proportion of high energy particles is greatest near the shower axis so ε must change with r . Nevertheless, it is legitimate as a first approximation to treat ε as constant. Accordingly, the effective number of shower tracks within a circle of radius R is

$$N' = \int_0^R \varepsilon \Delta 2\pi r dr = 2\pi R \varepsilon N/500$$

From Gauss's theorem $2\pi R \mathcal{E}_v^\perp = 2\pi K N'$ (symmetry ensures that $\mathcal{E}_v$ is perpendicular to the circular path). So

$$\mathcal{E}_v = 2\pi K \varepsilon N/500 = 8\pi 10^{-8} \varepsilon N \text{ } \mu\text{V m}^{-1} \text{ MHz}^{-1}$$

Within the approximations ($R < 40$ metres, ε independent of R) the field strength is independent of R . As before $E_p = 2 \times 10^9 N$ so

$$\mathcal{E}_v = 10^{-16} \varepsilon E_p \text{ } \mu\text{V m}^{-1} \text{ MHz}^{-1}$$

With an estimated $\varepsilon = 0.1$ and $E_p = 10^{17}$ eV, $\mathcal{E}_v \approx 1 \text{ } \mu\text{V m}^{-1} \text{ MHz}^{-1}$. The change from N to E_p is less sure here than in the previous calculation. The number of particles in a real shower of energy E_p is N only at the point of maximum development, whereas $\mathcal{E}_v$ has been calculated for N tracks of infinite length. I expect the extra track length used in the calculation to give an extra contribution to the calculated $\mathcal{E}_v$: in other words, the value is a generous upper limit to the true value. Other factors have also been ignored that will reduce the true $\mathcal{E}_v$. In particular the time lags between different particles in the shower front are typically 10–100 ns (ref. 1), and lead to a loss of coherence at frequencies ≥ 1 MHz.

In summary, if there were no coherent transverse deflexion of shower particles, such as is produced by the geomagnetic field, the radio frequency field from a shower of 10^{17} eV would certainly be less than $1 \text{ } \mu\text{V m}^{-1} \text{ MHz}^{-1}$. Geomagnetic deflexion¹ is expected to give fields of several $\mu\text{V m}^{-1} \text{ MHz}^{-1}$. Only on the most extreme, implausible, assumptions about the transverse deflexions is it possible to envisage fields of $\sim 100 \text{ } \mu\text{V m}^{-1} \text{ MHz}^{-1}$ at a frequency of 5 MHz. This upper limit is proportional to v , and therefore becomes smaller as frequency is reduced. Values near $10 \text{ } \mu\text{V m}^{-1} \text{ MHz}^{-1}$ might be observed experimentally, but fields as large as the quoted $1 \text{ mV m}^{-1} \text{ MHz}^{-1}$ appear to be completely ruled out.

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Recent Climatic Change and Increased Glacierization in the Eastern Canadian Arctic

THE climatic warming trend since the 1880s (refs. 1–5), which seems to have been global in extent and was manifested by an upward trend in mean annual (and particularly mean winter) temperatures, seems to have given way since the 1940s to a cooling trend⁶, which is most marked in higher latitudes ($> 60^\circ \text{N}$, refs. 7 and 8). Here we report recent field work on Baffin Island, eastern Canadian Arctic, and an analysis of the available climatic data for that area which provides further information.

We calculated seasonal running means of temperature and precipitation for all major weather stations on Baffin Island (Fig. 1). For the period 1960 to 1969 a marked decrease, by as much as 2.1°C , in the mean temperature of the ablation season (June to August) is apparent; but the accumulation season (September to May) shows an equally marked increase in temperature, by as much as 2.0°C . This pattern holds for all but two of the stations on Baffin Island (Table 1). The two exceptions are a result of local conditions at each site (Cape Dyer and Frobisher Bay).

An equally striking trend is seen for the seasonal precipitation totals over the same ten year period. Winter precipitation shows marked increases throughout Baffin Island, but summer records show more station to station variability (Table 1). In view of the extremely important influence of local topographic factors on precipitation in the area, the consistency of the trends over such a large area, where total precipitation amounts vary widely, is surprisingly good.

Using a catalogue of synoptic pressure pattern types for Baffin Island⁹, we examined airflow characteristics for the months of July and August. From 1961–1965 to 1966–1970 there was a 29% increase in the number of days on which airflow with an easterly (particularly a north-easterly) component affected the region and a concurrent decrease in the number of days on which airflow with a westerly (particularly a south-westerly) component affected the region. The increased frequency of cool air being advected into the area from the east and north-east has apparently resulted in lower summer temperatures. A synoptic classification catalogue for all of the winter months is not yet available but it seems likely that

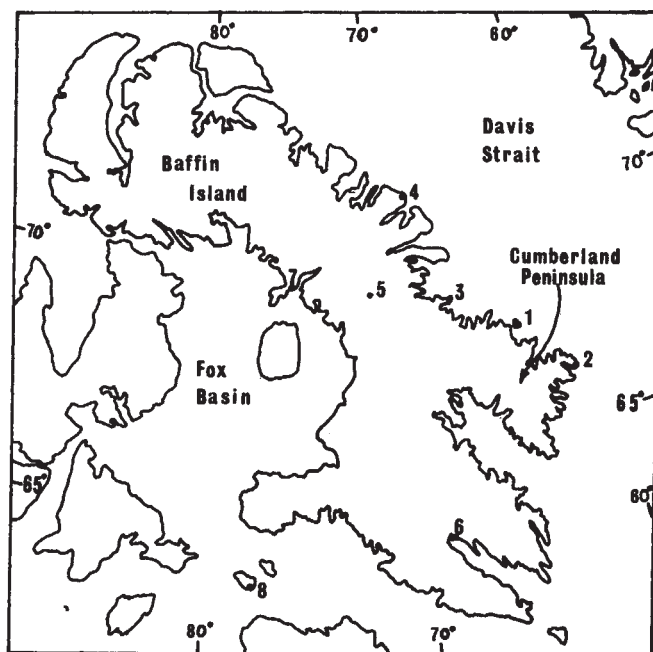


Fig. 1 Location of field area and meteorological stations discussed in text. Numbers refer to stations in Table 1.

Table 1 Net Changes in Seasonal Mean Temperatures and Seasonal Precipitation Totals, 1960–1969, derived from Linear Regressions

Station	Latitude	Longitude	Elevation (m)	Ablation season (J, J, A)			Accumulation season (Sept.–May)		
				Temperature change (° C)	Precip. (cm/we)	Change %	Temperature change (° C)	Precip. (cm/we)	Change %
1. Broughton Is.	67° 33'	64° 03'	581	−0.9	−0.2	−3.4	+0.7	+12.6	+51.7
2. Cape Dyer	66° 35'	61° 37'	376	−2.0	−6.9	−49.7	−0.4	+11.8	+21.8
3. Cape Hooper	68° 26'	66° 47'	401	−0.5	+5.8	+82.5	+0.4	+23.4	+127.4
4. Clyde	70° 27'	68° 33'	3	−2.1	−0.2	−2.2	+1.6	+2.2	+16.6
5. Dewar Lakes	68° 39'	71° 10'	518	−1.4	+0.2	+1.9	+0.9	+2.5	+23.3
6. Frobisher Bay	63° 45'	68° 33'	21	+0.03	−0.2	−1.3	+1.2	−2.6	−10.0
7. Longstaff Bluff	68° 57'	76° 18'	162	−2.1	−2.1	−24.9	+0.7	+0.7	+5.9
8. Nottingham Is.	63° 07'	77° 56'	16	−1.7	+3.7	+54.4	+2.0	+5.8	+32.9
Average				−1.3	+0.5	+7.2	+0.9	+7.1	+33.7

* Values are for net precipitation changes, 1960–1969, as a percentage of the mean 1960–1969.

the observed warming during these months is related to a higher frequency of days on which relatively warm, moist southerly air entered the region.

Short term climatic changes are manifested visually, by field evidence, only in sensitive regions. On Baffin Island, permanent snowbanks, incipient glaciers and the duration of ice cover on small lakes respond essentially concurrently with climate. Field observations (1969 to 1971) of these features in the northern Cumberland Peninsula (Fig. 1) and comparisons with aerial photographs taken late in the ablation seasons of 1949 and 1960 support the climatological evidence for a climatic deterioration.

Aerial photograph comparisons show that snowbanks generally decreased in area between 1949 and 1960, whereas all observed snowbanks increased markedly during the past decade. The actual increases are variable; permanent snowbanks now exist in many areas that were free from snow in 1960 and many of the smaller (<10 m diameter) snowbanks have more than doubled in size, whereas larger (>50 m diameter) snowbanks have changed less noticeably. In one instance, snowbanks now occupying an area free from snow in 1960 are encroaching on 25 mm diameter thalli of the lichen species *Alectoria minuscula*. A growth curve developed for this species, relating thallus diameter to substrate age, indicates a seasonally snow-free substrate for the previous 40 ± 10 yr (ref. 10). This suggests that the present distribution of snow cover, resulting from climatic deterioration over the past decade, is at least as extensive as that of 40 yr ago. In contrast to snowbank growth, glacier termini had receded between 1949 and 1960 and continued active recession through 1971 because of their much longer response time to climate.

Another, less frequently observed result of climatic change is the formation of incipient glaciers. In 1970 two cirques, which were snow-free in 1960, were noted as being occupied by glacierets or large snowbanks. Also, a number of small lakes (<1 km²) free from ice in 1960 have been observed to remain ice covered throughout the ablation season in recent years, and on many of these lakes ice has accumulated for several years. On all lakes observed, the percentage of ice-cover at the end of the ablation season was equal to or greater than ice-cover in 1960.

Williams *et al.*¹¹ have demonstrated the glaciological sensitivity of Baffin Island to climatic fluctuations. For an area north of the Barnes Ice Cap, Ives¹² has shown that although 2% of the area is now glacierized, in the recent past (<330 ± 75 yr (ref. 13)) 70% of the area was glacierized. The present glaciation limit for the area lies 0 to 300 m above the land surface¹⁴. Using an observed mean lapse rate for the area of 0.5° C/100 m based on radiosonde data (R. S. Bradley, unpublished), a mean summer cooling of 1.5° C, augmented by increased snowfall, seems sufficient to lower the glaciation limit below a significant portion of the land surface. An increase in the number and size of thin ice caps on the plateau region, and accompanying increases in the mean albedo of

the island during the ablation season, would give positive feedback and further reinforce the climatic trends already in progress.

Namias¹⁵ suggests that a new climatic regime over the North Pacific and North America began “abruptly in the late summer and fall of 1961”, as a result of warmer water replacing cold surface water in the central northern Pacific Ocean. This oceanic temperature anomaly has had the effect of amplifying the standing long wave pressure pattern in the Northern Hemisphere. Baffin Island is situated in a critical position with regard to the mean position of the upper air trough over eastern North America and slight changes in the position of the trough may significantly affect the climate of the region. So it is possible that the recent climatic fluctuation which has occurred in Baffin Island since the late 1950s is related to atmospheric teleconnections¹⁶ resulting from the inception of a new climatic regime which in turn can be related to large scale seasonal ocean–atmosphere interactions in the Pacific.

It is clear that the apparent cooling trend since the 1940s is not observed at present in this area. During the past decade mean annual temperatures on Baffin Island have been increasing, but the net effect on the landscape is an apparent move towards more glacial conditions. This contradicts assertions^{17,18} that a decrease in mean annual temperature is a prerequisite for increased glaciation of an area.

Finally, one may speculate on the glaciological implications of a continuation of this trend towards more accumulation of snow and ice on the land. According to Namias¹⁹ “there seems to be no strong reason why repetitive conditions such as those described cannot lead to climatic fluctuations of a much longer time scale than a decade”. Should the present circulation regime be maintained for, say, another ten years, then dramatic changes in the pattern of accumulation in the area can be expected following the lag response to a lowering of the glaciation limit.

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Formation of the Earth's Core

In the conventional view of core formation the Earth accreted from a homogeneous mixture of iron and silicates, and the core formed when radioactive heating melted the iron which subsequently drained toward the centre¹, the change in gravitational potential energy increasing the average temperature of the Earth by some 2,000 K. In these circumstances core formation would be the major event in the thermal evolution of the Earth².

Assuming the Earth accreted uniformly with respect to composition 4.5×10^4 yr ago, we have concluded that core formation could have been simultaneous with the accretion process³. The initial temperatures necessary to lead to core formation, together with the temperature rise on core formation, would generate temperatures greater than 3,000 K in most of the planet, lending further credibility to the "hot origin" theory. Earlier, Ringwood⁴ had inferred a "hot origin" for the Earth, as well as core formation on accretion, by geochemical arguments.

The conventional view of core formation within an originally homogeneous Earth, however, is not so much the most attractive hypothesis as merely the simplest possible assumption. Turekian and Clark⁵ and Clark *et al.*⁶ have offered an alternative in which the Earth accreted inhomogeneously, material accumulating on the proto-Earth in the sequence from which it condenses out of the solar nebula. The core formed immediately from the high temperature condensate, iron, and was essentially intact before any important amount of silicates condensed. The difficulty with this model, however, is that there is insufficient energy, either gravitational or compressional, to melt the outer core on or after accretion; the core would remain solid because of the depletion, based on chemical and meteoritic evidence, of the heat producing radioactive elements in iron⁷. But the inhomogeneous accretion model is attractive because it helps to explain the chemical differences among the meteorites and among the terrestrial planets, including the Moon. We propose that the inhomogeneous accretion hypothesis, when looked at in more detail, can explain early melting of the core.

The condensation sequence of elements and compounds from a cooling cloud of solar composition has been considered in detail^{8,9}. The first compounds to condense are the Ca and Al rich oxides, silicates and titanates, which include MgAl_2O_4 , CaTiO_3 , Ca_2SiO_4 , Al_2SiO_5 , CaSiO_3 , $\text{CaMgSi}_2\text{O}_6$, $\text{Ca}_2\text{Al}_2\text{SiO}_7$, $\text{Ca}_3\text{MgSi}_2\text{O}_8$ and $\text{Ca}_2\text{MgSi}_2\text{O}_7$, all of which condense at temperatures above the inhomogeneous condensation of iron⁹. CaTiO_3 , MgAl_2O_4 , Al_2SiO_5 and $\text{CaAl}_2\text{Si}_2\text{O}_8$ condense before Fe even under equilibrium conditions. Uranium, thorium, and the rare earth elements (REE) are also refractory and can be expected to condense early. For example, Ca-rich achondrites are high in Ca, Al, Ti, U, Th, and REE relative to the chondrites, and it has been proposed that these

meteorites represent high temperature condensates or a differentiate of such a condensate^{8,10}. They are low in Fe and volatile fractions and presumably accreted before significant iron had condensed in their vicinity. The Moon also has these chemical characteristics and an origin in terms of a high temperature condensation process is appropriate for that body as well¹¹. Such an origin for the Moon explains the Ca-Al enrichment at the lunar surface and interior¹¹, the U, Th, and REE enrichment of the surface and the deficiency in volatiles.

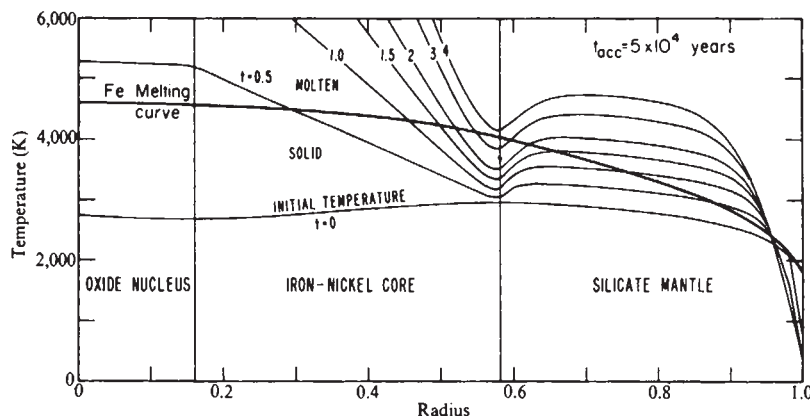
In our model the nucleus of the proto-Earth consists of the early high temperature condensates and is rich in Ca, Al, Ti, Th, U, and REE. The Moon and the calcium-rich achondrites may be taken as prototypes. The uranium content of these bodies is much higher than chondritic abundances. In particular, the eucrites, a class of Ca-rich achondrites, have U concentrations an order of magnitude larger than carbonaceous chondrites. The Ca-rich inclusions in the Type III carbonaceous chondrites¹² may represent an even more primitive condensate and differentiation of such material may be the source of eucrites and lunar basalts and anorthosites. These are also deficient in Fe and enriched in rare earths and, by analogy, in U. Iron condenses and accretes after the formation of the highly radioactive nucleus; the planet Mercury presumably accreted to this stage. Important mantle minerals such as MgSiO_2 and Mg_2SiO_4 condense and accrete later. Potassium, another important heat producing element, becomes significant at the later stages of accretion, as do the volatiles such as H_2O and FeS.

The presence of a radioactive nucleus provides a mechanism for melting the iron core. For illustration we have taken a very simple model for the primordial layering in the Earth. We assume that the refractory nucleus has the composition of eucrites and accreted before iron. The Ca-rich inclusions of Type III carbonaceous chondrites may be a better analogue of the primitive condensate, but their U and Th contents have not been measured. The size is somewhat arbitrary. It is presumably at least as large as the Moon and its size may be related to the present size of the solid inner core. We assume that a mixture of iron and eucritic material accretes on the nucleus to form the protocore and that the radioactivity decreases linearly from eucritic values at the top of the nucleus to zero at the top of the iron-rich shell. The mantle accretes later and has the radioactive abundances of chondrites. An accretion time of 5×10^4 yr is assumed with the Hanks-Anderson³ accretion rate. The initial temperature profile is calculated from Larimer and Anders's condensation temperatures, the assumption of radiative equilibrium during accretion and adiabatic compression in the interior (Fig. 1). We note that the initial temperatures are well below the melting curve for iron in the iron regions of the Earth. Faster accretion can increase the initial temperatures, of course, but the accretion time should not be less than the cooling time of the nebula, an upper limit for which has been estimated to be 10^4 yr (ref. 6). The central part of the body is relatively cold in any case.

The iron core was presumably at least partially molten 3×10^9 yr or longer ago judging from the remanent magnetism in ancient rocks. In our model melting of iron commences at about 0.4×10^9 yr, and it would begin earlier and proceed more rapidly for shorter accretion times. We have ignored latent heats of melting and convection; the very large temperature rise in the deep interior is caused by the high radioactivity in this region. We have adopted the values $U = 9.1 \times 10^{-8}$ g/g, $\text{Th}/U = 4$ and $\text{K}/U = 2 \times 10^3$ for the nucleus. The temperature minimum at the core mantle boundary is a consequence of the zero concentration of U, Th and K assumed there. So early melting of the iron core is a consequence of the properties of the initial condensates.

The nucleus and the protocore are not in gravitational equilibrium because iron is denser than the nucleus. As melting of the iron commences the nucleus, if perturbed, will attempt to rise, either in fragments or *in toto*. The rise of the nucleus to the top of the molten iron zone and, eventually, to

Fig. 1 Temperatures as a function of radius and time for an Earth model that accretes in 5×10^4 yr during condensation. The radius coordinate is fractions of the Earth's radius. Temperature curves are at intervals of half-billion years after accretion 4.5×10^9 yr ago. Initial temperatures are computed from the condensation temperature, radiative equilibrium during growth and adiabatic compression. The melting curve for iron is from Higgins and Kennedy¹⁹. The radioactivity of the nucleus and the mantle is eucritic and chondritic, respectively. The radioactivity of the iron shell decreases from eucritic to zero.



the base of the mantle will not be symmetric because of the convective pattern in the core which is controlled by the rotation of the Earth. The nucleus will presumably rise preferentially along one of the poles of rotation.

When the nucleus leaves the centre of the Earth it will be replaced by nickel-iron which, before its descent, is close to its melting point. Because of the steep slope of the melting curve relative to the adiabatic compression curve it will refreeze; this explains the seismic evidence regarding the solidity and the composition of the inner core. The release of gravitational energy resulting from the overturn of the original nucleus-core configuration should result in an average temperature rise of not more than several hundred K. The present size of the inner core may therefore represent the initial size of the nucleus.

The solidity of the inner core was inferred initially from indirect arguments and was verified in 1968 by free oscillation calculations^{13,14}. It has a very high Poisson ratio, consistent with its high temperature and pressure^{6,15}. The density and velocity jump from the outer to the inner core implies that the inner and outer cores are not of the same composition; the inner core is deficient in the low density, high velocity alloying component. Its properties are consistent with solid iron-nickel. Our model leads us to suggest that part of the extra material in the molten outer core may be residue from the nucleus, that is, Ca-Al rich oxides and silicates either in solution or in suspension. If so, the high radioactivity of this material may provide part of the energy for driving the dynamo.

We estimate that the density of the nucleus at the core-mantle boundary will be less than the density of the "normal" mantle at this boundary. This, together with its high radioactive content, provides mechanisms by which it might melt its way to the Earth's surface and initiate continental growth, preferentially in one hemisphere, some 3.8×10^9 yr ago. The change in the U/Pb ratio at 4.1×10^9 yr (ref. 20) and the Precambrian anorthosite event²¹ may also be related to the emergence of the nucleus. As noted earlier, anorthosite is one of the early condensates. Such an emergence of the protonucleus clearly depends on the early mechanical properties of the mantle.

The size of the nucleus is about 2 to 3% of the mass of the Earth. This is approximately the amount of material that condenses from a cloud of solar or chondritic composition before iron. For comparison the continental crust accounts for 0.35% of the Earth and the lower mantle transition region for 1.5 to 3%. Residual protonuclear material, mixed with iron, may account for the properties of the transition region. We would expect the transition region to vary in thickness and, perhaps, to be entirely missing in some regions. This would lead to topography at the core-mantle boundary, a feature that is desired to explain certain features of the Earth's gravity and magnetic fields^{16,17}. The presence of patches of Ca-Al-U rich silicate material at the base of the mantle may also be the source of deep mantle convection plumes and hot spots¹⁸.

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Search for Fine Structure in the K_{13}^0 Final States

INTEREST in leptonic resonances has been generated recently by both experimental and theoretical investigations^{1,2}. Anomalies in bubble chamber data have indicated a possible $\pi^\pm \mu^\mp$ resonance of mass ≈ 429 MeV and width < 15 MeV in the final state of both $\nu p \rightarrow \pi \mu p$ interactions and $K_L^0 \rightarrow \pi \mu \nu$ decays¹. Theoretical estimates of the effects of such a resonance have been made (S. C. Chhajlany and S. Pakvasa, unpublished), and it has been suggested (S. Barshay, unpublished) that the low measured limit on the rate for $K_L^0 \rightarrow \mu^+ \mu^-$ (refs. 3 and 4)

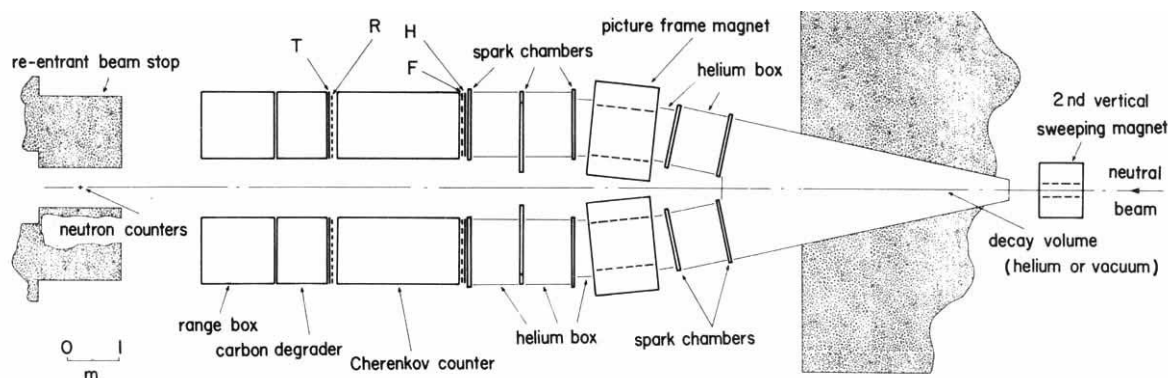


Fig. 1 Plan view of the apparatus. The apparatus is symmetric about the neutral beam centre line. F and R, Scintillation counter hodoscopes; H, a six-counter array; T, a fast-timing counter.

could be a consequence of an interfering $\pi\mu$ intermediate state. Studies of finite quantum field theory with an indefinite metric suggest (E. C. G. Sudarshan, unpublished) that leptonic resonances, if they exist, could manifest themselves in γe , πe , $\pi\mu$ and $\pi\nu$ channels.

The data reported here consist of more than 100,000 analysed $K_{\mu 3}$ events and 200,000 $K_{e 3}$ events. A plan view of the detection apparatus is shown in Fig. 1. The spectrometer was originally designed to search for K_L^0 decays into lepton pairs^{3,4}. The region of the Dalitz plot examined in this data sample was determined by setting the field integral of the spectrometer magnets to correspond to a transverse momentum of 180 MeV/c.

The trigger logic required a particle to count in the H array in one spectrometer arm and a coincident particle to register as a "lepton" in the other arm. For the trigger, a "lepton" was defined as a particle which was parallel to the neutral beam line within ± 45 mrad (as determined by the hodoscopes F and R), and which was identified either as an electron by counting in the Čerenkov counter (freon-12 at 1 atm) or as a

possible muon by penetrating beyond the second counter in the range box (corresponding to a minimum muon momentum of 550 MeV/c). The spark chamber and counter information was checked with an on-line PDP 9 computer and stored on magnetic tape for later analysis on a CDC 6600 computer. The experimental conditions were such that the data reported here were accumulated in less than 24 h.

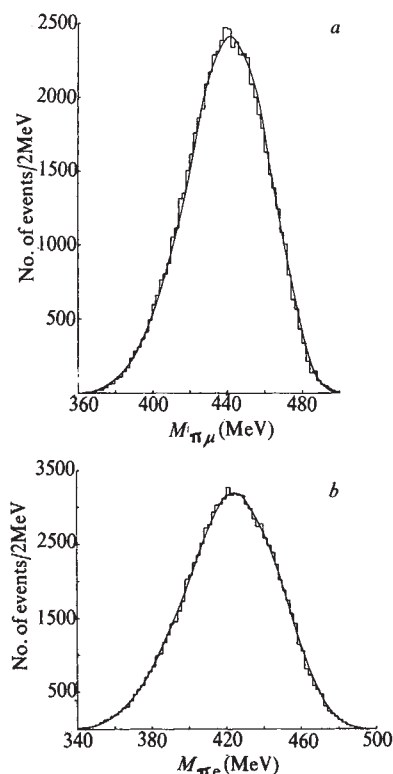


Fig. 2 a, The $\pi\mu$ invariant mass spectrum from the data for $K_L^0 \rightarrow \pi + \mu + \nu$; b, the πe invariant mass spectrum from the data for $K_L^0 \rightarrow \pi + e + \nu$. The smooth curves are from V-A theory (see text).

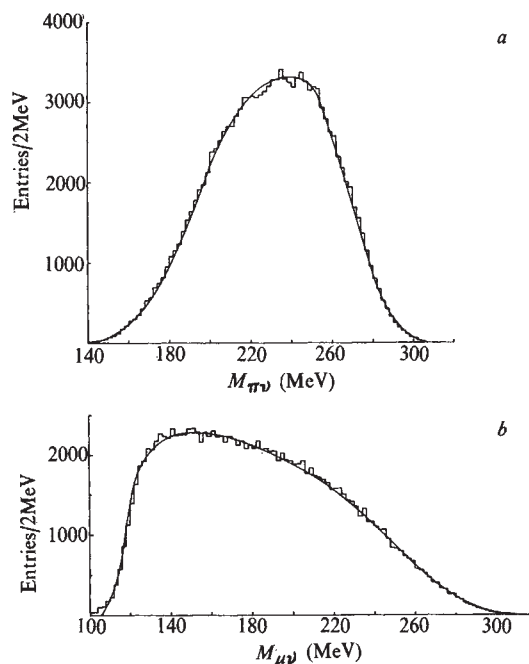


Fig. 3 Invariant mass spectra for the decay $K_L^0 \rightarrow \pi + \mu + \nu$. a, $\pi\nu$ mass spectrum; b, $\mu\nu$ mass spectrum. The smooth curves are from V-A theory (see text). Each event is plotted twice in each diagram.

The reconstructed events were required to pass cuts on trajectory continuity on each side, vertex reconstruction, and kinematic consistency with the assumed decay. In addition, range cuts were applied to ensure that the secondary particles were properly identified; a muon had to stop within 20% of its expected range and a pion had to stop more than 30% short of the expected range of a muon of the same momentum. Thus all $K_{L 3}$ events had a pion which was clearly identified because it either interacted in the absorber or decayed in flight. Events which were consistent with $K_L^0 \rightarrow \pi^+ \pi^-$ decay were eliminated from the $K_{\mu 3}$ spectra.

The histograms of Figs. 2 to 4 show the final πl , $\pi\nu$ and $l\nu$ mass spectra for the $K_{\mu 3}$ and $K_{e 3}$ data. Because the charged secondary particle momenta and directions were measured, the $M_{\pi e}$ spectrum from $K_{e 3}$ and the $M_{\pi\mu}$ spectrum from $K_{\mu 3}$

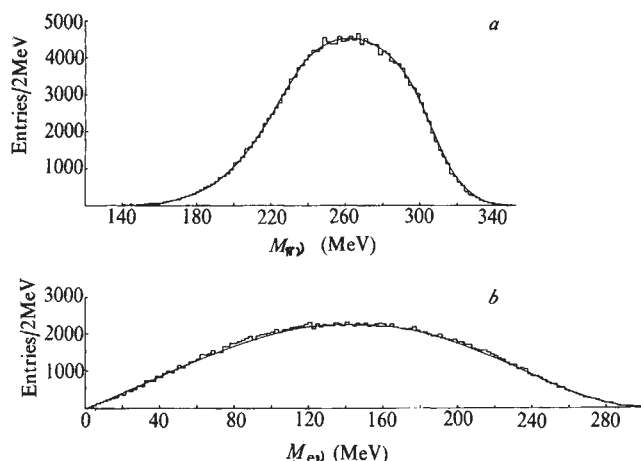


Fig. 4 Invariant mass spectra for the decay $K_L^0 \rightarrow \pi + e + \nu$. *a*, $\pi\nu$ mass spectrum; *b*, $e\nu$ mass spectrum. The smooth curves are from V-A theory (see text). Each event is plotted twice in each diagram.

decays are computed directly. But, because only the direction of the kaon is known, each event has two kinematically acceptable solutions for the neutrino vector momentum. Thus each event is plotted twice for the $M_{\pi\nu}$ and $M_{e\nu}$ spectra from $K_{\mu 3}$ events, and for the $M_{\pi\mu}$ and $M_{e\nu}$ spectra from $K_{e 3}$ events. The resolution of the apparatus and the absolute invariant mass calibration were determined from an analysis of $K_L^0 \rightarrow \pi^+ \pi^-$ events taken simultaneously with the $K_{\mu 3}$ and $K_{e 3}$ events. The resolution (FWHM) is less than 4 MeV for the $M_{\pi\mu}$ and $M_{\pi e}$ distributions.

The smooth curves in Figs. 2 to 4 are the predictions of the V-A theory folded with the calculated acceptance of our equipment; the factors assumed were $\xi(0) = -0.8$, $\lambda_+ = 0.04$ and $\lambda_- = 0$. For reasons of economy, the efficiency calculations were done with variables appropriate to the $\pi\mu$ and πe mass spectra, and it was necessary to smooth the curves shown with the $\pi\nu$, $e\nu$ and $\mu\nu$ data. Accordingly, the curves shown in Figs. 3 and 4 were not used to check for deviations from the V-A theory; nevertheless the computed predictions agree quite well with the data.

To estimate the contributions from a $\pi\mu$ resonance as reported in ref. 1, we have compared the measured $M_{\pi\mu}$ spectrum with the V-A spectrum plus a Breit-Wigner enhancement of width 15 MeV. We see no evidence for an enhancement in our data, with an upper limit on the branching ratio

$$\frac{\Gamma(K_L^0 \rightarrow \mu^+ (429) + \nu \rightarrow \pi^\pm + \mu^\mp + \nu)}{\Gamma(K_L^0 \rightarrow \text{all})} < 3 \times 10^{-4} \quad (90\% \text{ confidence level})$$

This limit is two orders of magnitude lower than the branching ratio estimate given in ref. 1 for the $K_{\mu 3}^0$ data. If the structure is assumed to be something other than a final state resonance, it seems unlikely that the effect would be seen in the bubble chamber data or in this experimental search which has better resolution, positive particle identification, and thirty times as many data in the region of interest.

The observed anomalies may be correlated with the angle $\theta_{\mu\nu}$ between the muon and the neutrino as measured in the $\pi\mu$ centre-of-mass frame¹. The $\theta_{\mu\nu}$ distributions (not shown) for the $K_{\mu 3}$ data shown in Fig. 2 have been compared with the Monte Carlo calculations. In all cases the $\theta_{\mu\nu}$ distributions vary smoothly as the $M_{\pi\mu}$ interval changes and agree well with the V-A predictions. Also the relative detection efficiency as a function of $\theta_{\mu\nu}$ for any $M_{\pi\mu}$ near the reported enhancement does not vary by more than $\pm 30\%$; thus the contradiction between the bubble chamber results and those reported here cannot be attributed to a difference in detection efficiencies.

As well as the test described above on the $\pi\mu$ data, each spectrum was tested for smoothness. For bin widths of 10,

6 and 2 MeV, deviations of each bin from a curve through six neighbouring bins have been examined for all the spectra. In addition, the $\pi\mu$ and πe spectra were treated in bins of width 20 MeV to check for the effect reported in ref. 1. (The analysis was carried out twice, with the bins offset by 10 MeV.) In all, 600 bins have been examined, and only four have been found to deviate from a smooth curve by more than three standard deviations, the largest deviation being 3.7 standard deviations. From this analysis there is no statistically significant evidence for structure narrower than 10 MeV in any of the mass spectra, or 20 MeV in the $\pi\mu$ and πe spectra.

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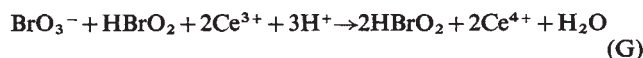
Explanation of Spatial Band Propagation in the Belousov Reaction

BELOUSOV¹ reported that the ratio $[\text{Ce(IV)}]/[\text{Ce(III)}]$ undergoes repeated temporal oscillations in a stirred sulphuric acid solution containing bromate ion and malonic acid. Busse² and Zaikin and Zhabotinsky³ reported that spatial bands of alternating oxidizing and reducing character propagated through an unstirred solution if it were initially subject to a concentration gradient. Existence of these bands was demonstrated by the redox indicator ferroin (the 1,10-phenanthroline complex of ferrous ion), and bands could be generated in the absence of cerium ions if indicator were present, because the ferroin indicator itself serves as an oxidation-reduction couple in the absence of cerium ions.

Winfree⁴ has described the remarkable two-dimensional behaviour pattern by which narrow circular bands of oxidation with sharp leading edges and diffuse trailing edges propagate through the solution at velocities of the order of mm/min. The bands are generated at centres of oscillation, called pacemakers, which are probably heterogeneous in nature. Following bands never overtake those in front of them, but bands coming from opposite directions from different pacemakers annihilate each other. Bands disappear without reflexion at the boundaries of the system. If bands are broken by agitation of the solution, revolving spiral band systems develop about the resulting discontinuities.

Field, Körös and Noyes (see ref. 5 and unpublished work) have elucidated the detailed molecular mechanism of the temporal oscillations in a uniform solution, and the same reactions permit a qualitative explanation of the spatial bands described by Winfree⁴. Numbering of reactions is taken from the previous papers (see ref. 5 and unpublished work).

The leading edge of an oxidizing band advances into a reducing region containing bromide ion somewhat in excess of 10^{-6} M. Within the leading edge, bromous acid is generated autocatalytically by the net process (G).



Reaction (G) is the sum of reactions (R5) + 2(R6), where (R5) is rate determining



The resulting HBrO_2 reacts further by the sequence (R4) + (R8a)



Thus the net reaction in the advancing band front is (B)



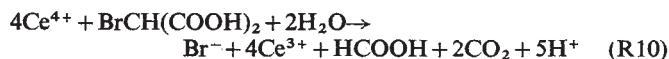
It is the sudden appearance of the oxidized Ce^{4+} in the leading edge of the advancing band that causes the sharp colour change of the indicator.

HBrO_2 and Br^- destroy each other by (R2)



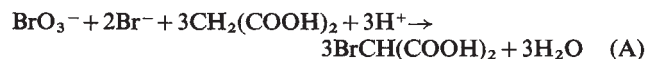
and this reaction inhibits the autocatalytic process (G) until the concentration of Br^- has been reduced to a critical value. Interdiffusion of these species across the advancing band front destroys Br^- and triggers the autocatalytic production of HBrO_2 by process (G) in the area into which the band is moving. The autocatalytic nature of process (G) causes the band to advance much more rapidly than would a diffusion process driving an excess of one species into a solution of a potential reactant, but the velocity of propagation is related inversely to the ambient Br^- concentration.

Immediately behind the leading edge of a band, the accumulating Ce^{4+} begins to react with bromomalonic acid by reaction (R10).



When the rate of this reaction becomes great enough, reaction (R2) destroys HBrO_2 more rapidly than it is able to regenerate itself by the autocatalytic process (G), and the concentration of this species falls very rapidly. Ce^{4+} is no longer formed, and its concentration is steadily reduced by reaction (R10) while the colour of the indicator changes from the oxidized to the reduced form in the diffuse trailing edge of the band.

At the same time that Ce^{4+} is being consumed, Br^- is being depleted by net process (A).



This process is initiated by the rate-determining reaction of BrO_3^- and Br^- ions. The concentration of Br^- would eventually be reduced by process (A) to the point that the solution at some specific distance behind the band would undergo a temporal oscillation (ref. 5 and unpublished results) and thereby initiate a following band. Alternatively, the pace-

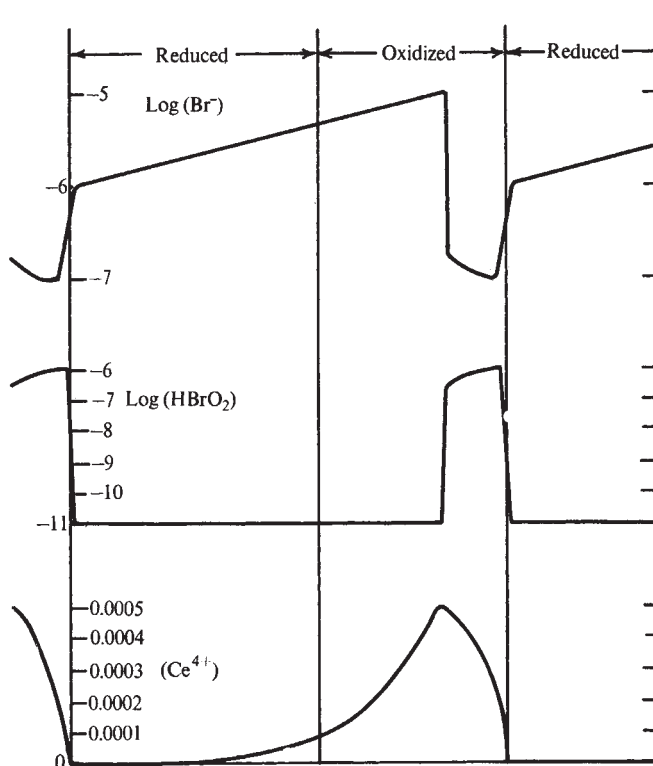


Fig. 1 Approximate concentration profiles for Br^- and HBrO_2 (logarithmic scales) and for Ce^{4+} (linear scale) in a typical train of bands moving from left to right.

maker may generate new bands at a frequency greater than the spontaneous one. If the frequency of the pacemaker is greater than that for bulk oscillation in the medium, temporal oscillations will be suppressed in a constantly increasing area of concentric expanding bands.

Fig. 1 illustrates the concentration behaviour of the key species Br^- , HBrO_2 and Ce^{4+} in one of a series of advancing bands. Each band moves through the solution by destroying Br^- in the region in front of it, yet the concentration of Br^- in its wake is greater than that in front of it. This remarkable behaviour was predicted by Winfree⁴.

Because each band leaves behind itself a region unfavourable for propagation of a band, a trailing band will never overtake a leading one, and a band will not be reflected by a physical obstruction. Two bands converging on the same region by destroying Br^- will obviously annihilate each other when they meet. If an outermost band is advancing into a nearly uniform region in which the concentration of Br^- becomes so small that it undergoes an oxidizing pulse (ref. 5 and unpublished results), this band will have been destroyed when the region becomes reducing again, but interior bands will be unaffected.

Because reaction (R10) is strongly exothermic, the temperature increases in an oxidizing band and the density of the solution there is less than in a reducing band. Undoubtedly this effect is responsible for the observation of Busse² that bands in a bulk medium tend to be horizontal.

My discussion has been restricted to bands of oxidizing solution that are either continuous (for example, circular), or that terminate at the walls of the container. If, however, a band in a two-dimensional system is broken, the directional propagation of the area of oxidation will cause the advancing band front to rotate about the discontinuity with a characteristic frequency, thereby generating a spiral band system as reported by Winfree⁴.

The above qualitative explanation appears to be entirely consistent with prior observations of bulk² and of two-dimensional^{3,4} systems and with our own description (ref. 5 and unpublished work) of the behaviour of the Belousov reaction in a homogeneous system. We are developing a more quanti-

tative description of these space bands and will discuss the implications of some of their remarkable properties.

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Water Molecule in Hydrophobic Surroundings: Structure of α -Cyclodextrin-Hexahydrate ($C_6H_{10}O_5$)₆ · 6H₂O

α -CYCLODEXTRIN (cyclohexaamylose) is the smallest member of the family of Schardinger dextrins, a group of cyclic D-glucosyl oligosaccharides each consisting of six to nine α -(1 $\rightarrow$ 4) linked glycopyranoses. These torus shaped molecules have voids of approximate diameter 6–9 Å and are capable of forming inclusion complexes with a variety of "guest" molecules^{1,2}. In the crystalline state, these complexes can exist as either "cage" or "channel" structures, depending on whether the cyclodextrins align themselves so that the voids form continuous, extended channels. At least eight different, non-isomorphous crystalline modifications of α -cyclodextrin with various different guest molecules are known. Cyclodextrin inclusion complexes can also exist in aqueous solution. As it has been proposed³ that simultaneously with complex formation the included solvent (water) is released, for an understanding of the mechanism of complex formation it is important to determine how many and in what manner solvent molecules are bound to the interior of the cyclodextrin ring. The structure we report here is that of α -cyclodextrin · 6H₂O (α CDH₂O), the "empty" inclusion complex, and is of the cage type.

The space group is orthorhombic, P2₁2₁2₁, with unit cell dimensions $a = 14.856$ (3), $b = 33.991$ (13) and $c = 9.516$ (4) Å as determined from least squares refinement of 9 diffractometer measured 2 θ data ($2\theta \geq 50^\circ$; $\lambda = 1.5418$ Å). Assuming six water molecules per cyclodextrin molecule, and four formula units per cell [(C₆H₁₀O₅)₆ · 6H₂O, formula weight = 1,081], the calculated density is 1.494 g/cm³; the observed density (McMullan *et al.*, unpublished results) is 1.491 (2) g/cm³ (flotation method: hexane and methyl iodide). The intensities of 4,551 diffraction maxima were measured on a Siemens four circle diffractometer out to a maximum $2\theta = 130^\circ$. 9.2% of the measurements resulted in intensities less than three times the standard deviations of the measurements (estimated from counting statistics plus a 3% of I_{net} machine error allowance), and these reflexions were not included in the least squares refinement procedure.

Initial attempts to determine the α CDH₂O structure by the application of direct methods, or by full matrix or rigid body least squares refinement starting from the coordinates of the cyclodextrin molecule in the pseudoisomorphous cyclodextrin iodine complex (McMullan *et al.*, unpublished results), were unsuccessful. Full matrix least squares refinement, however, starting from the coordinates of the cyclodextrin in the iodine

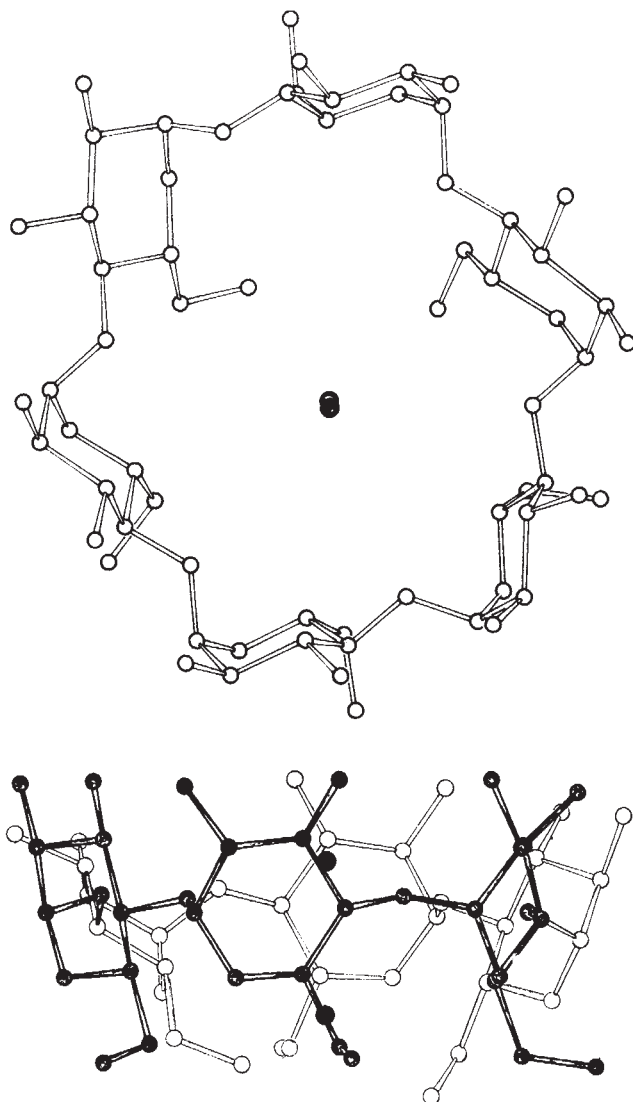


Fig. 1 α -Cyclodextrin · 6H₂O. The two included water molecules are shown as black circles. In the lower half of the figure, the side nearer the reader is shaded.

complex, omitting O₆ atoms, and using a limited data set of 977 reflexions ($2\theta \leq 60^\circ$ and/or $F_{obs} \geq 75$) slowly converged. The O₆ atoms and water molecules were later located from difference Fourier syntheses. Further block diagonal least squares refinement minimizing $\sum w(|F_{obs}| - |sF_{calc}|)^2$ where $w = 1/\sigma^2(F)$, including anisotropic temperature factor refinement, and not including in the structure factor calculation the contribution of the hydrogen atoms whose positions could be calculated has led thus far to a conventional $R = (\sum ||F_{obs}| - |sF_{calc}||) / \sum |F_{obs}|$ value of 0.082. Fig. 1 illustrates one molecule of the structure.

Each glucose unit is in the C1 chair conformation, and all glucose units are linked α -(1 $\rightarrow$ 4); this result is in agreement with the findings of Hybl, Rundle, and Williams⁴ for the non-isomorphous α CD-potassium acetate structure. From an examination of Kendrew wire models it is apparent that a hexagonally symmetrical configuration for α -cyclodextrin is strained. In α CDH₂O, four of the O₄ linking oxygen atoms lie very near the least squares mean plane of all six O₄ atoms, with deviations of 0.00, 0.07, 0.16, and 0.18 Å. The O₄ atom from one glucose is, however, displaced by 0.71 Å from the mean plane of all six O₄ atoms, and the O₄ atom of the adjacent glucose is displaced -0.98 Å, that is, toward the opposite side of the mean plane. The strain relief mechanism appears to be a rotation of a single glucose rather than a symmetrical

puckering. In the α CD-potassium acetate complex the cyclodextrin is located around a crystallographic two-fold axis, and all O_4 atoms are within 0.01 Å of the common mean plane. In the α CDI₂ structure pseudoisomorphous with the present α -CDH₂O, the maximum deviation is 0.19 Å. It appears that with only water as the included substance, the cyclodextrin torus can, to some extent, collapse.

Two water molecules are located inside the cyclodextrin ring; both are essentially on the mean molecular axis. The first is located approximately at the point where the mean plane through the six C_2 atoms intersects the axis, and the second between the points where the mean planes through the six C_5 and C_6 atoms intersect the axis. The first water molecule is probably hydrogen bonded to the second (O—O distance 2.84 Å), and the second is probably hydrogen bonded to at least one O_6 oxygen (2.74 Å) and is possibly bonded to another O_6 oxygen from a second glucose (3.01 Å). The first water molecule is not hydrogen bonded to any of the O_2 , O_3 or O_4 atoms of the enveloping cyclodextrin.

A full explanation of the hydrogen bonding scheme is not yet possible as the locations of the thirty hydroxyl and water hydrogen atoms have not yet been determined. The regular hydrogen bonding between oxygen atoms O_2 and O_3 of adjacent glucose residues inferred on the basis of O_2 — O_3 distances of about 2.85 Å consistently observed in the K^+ -acetate inclusion complex does not appear to be present in the case of α CDH₂O. In α CDH₂O, the O_2 — O_3 distances are 2.96, 3.02, 2.83, 3.36, 2.91 and 3.01 Å. With the exception of the one O_2 atom apparently hydrogen bonded to an adjacent O_3 atom (the 2.83 Å distance above), it appears to be possible to form a hydrogen bond between every O_2 or O_3 atom and either a water molecule or an oxygen atom of another cyclodextrin molecule. In the iodine complex it was observed also that hydrogen bonding between O_2 and O_3 of adjacent glucose residues in the same molecule is not always found. In α CDI₂, the appropriate O_2 — O_3 distances are 2.83, 3.22, 2.74, 3.00, 3.83 and 3.00 Å.

The differences in the cyclodextrin conformation, ring and the differences in the hydration structure presumably account for the anomalous density of α CDH₂O. The water complex is actually denser than the "pseudoisomorphous" n-propanol or n-butanol complex despite the low density of included material in the α CDH₂O structure. The unit cell volume of α CDH₂O is 4805 Å³ ($14.856 \times 33.991 \times 9.516$ Å) while that of α CD n-propanol is 5040 Å³ ($14.292 \times 37.515 \times 9.393$ Å) and that of the α CD n-butanol complex is 5140 Å³ ($14.392 \times 37.99 \times 9.14$ Å). The respective observed densities (McMullan *et al.*, unpublished results) are 1.491 (2), 1.468 (2) and 1.416 (2) g/cm³.

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BIOLOGICAL SCIENCES

Further Proof of Genetic Inactivation of the X Chromosome in the Female Mule

In the female mule (*Equus caballus* × *E. asinus*), the horse (maternal) and the donkey (paternal) X chromosomes are morphologically distinguishable^{1,2}, and the X-linked enzyme, glucose-6-phosphate dehydrogenase (G-6-PD), is present as a combination of the two electrophoretically distinct parental forms^{3,4}. Female mule cells therefore may serve as an experimental model for the simultaneous study of both cytological and biochemical aspects of dosage compensation for X-linked loci in mammals (Lyon hypothesis⁵). We have demonstrated a very close correlation between late replication of either one or the other of the parental X chromosomes, and relative activity of the complementary form of G-6-PD⁶. In this study we have obtained further and more rigorous proof that late replication of the X chromosome corresponds to genetic inactivation at the G-6-PD locus. We have also obtained data bearing on the problem of the postulated randomness of inactivation.

Table 1 Late Replicating X Chromosome and G-6-PD Type in Clones of Female Mule Fibroblasts

Animal	Clone	Late replicating X chromosome*	G-6-PD type % of total
251	C3	—	H-100
	C4	—	H-100
252	C1	X ^D (48)	H-100
	C2	X ^D (77)	H-100
	C3	—	D-100
	C4	—	H-100
267	C1	X ^D (54)	H-100
	C3	X ^D (70)	H-100
A36-1	C2	X ^D (44)	H-100
	C4	X ^H (62)	D-100
	C7	X ^D (58)	H-100
	C9	X ^H (26)	D-100
A36-2	C11	X ^H (38)	D-100
	C1	X ^H (44)	D-100
	C2	X ^D (53)	H-100
	C3	X ^D (50)	H-100
	C4	X ^D (47)	H-100
	C7	X ^H (47)	D-100
	C11	—	H-100

* In parentheses the number of cells analysed.

Fibroblast strains were established from skin biopsies from four female mules. The cultures were maintained in 250 ml. plastic tissue culture flasks in Ham's F-10 nutrient medium. Clones of fibroblasts were initiated from single cells by the method of Puck *et al.*⁷. Cells were prepared for chromosome analysis by a modification of the method of Moorhead *et al.*⁸. Autoradiography and G-6-PD quantification have been described in detail elsewhere⁶. G-6-PD electrophoresis was carried out at 4° C on cellulose acetate gel ('Cellogel'—Chemtron, Milan, Italy) buffered with 16 mM Tris; 3 mM EDTA; 7.5 mM boric acid, pH 7.8, containing 0.02 mM NADP. After brief incubation of the gels in the presence of 0.66 mM NADP, 1.2 mM G-6-P, 0.33 mM MgCl₂, and 0.33 M Tris-HCl buffer (pH 8.0), the fluorescent bands were excised from the gel and eluted in buffer; enzyme activity was assayed spectrophotometrically or fluorometrically. This technique is sensitive enough to reveal the presence of <5% of either parental enzyme form in the presence of the other.

Of nineteen clones examined, fourteen were studied simultaneously by cytological and biochemical techniques (Table 1). In nine clones, the donkey X chromosome was late replicating in all cells examined, and the horse-type G-6-PD represented

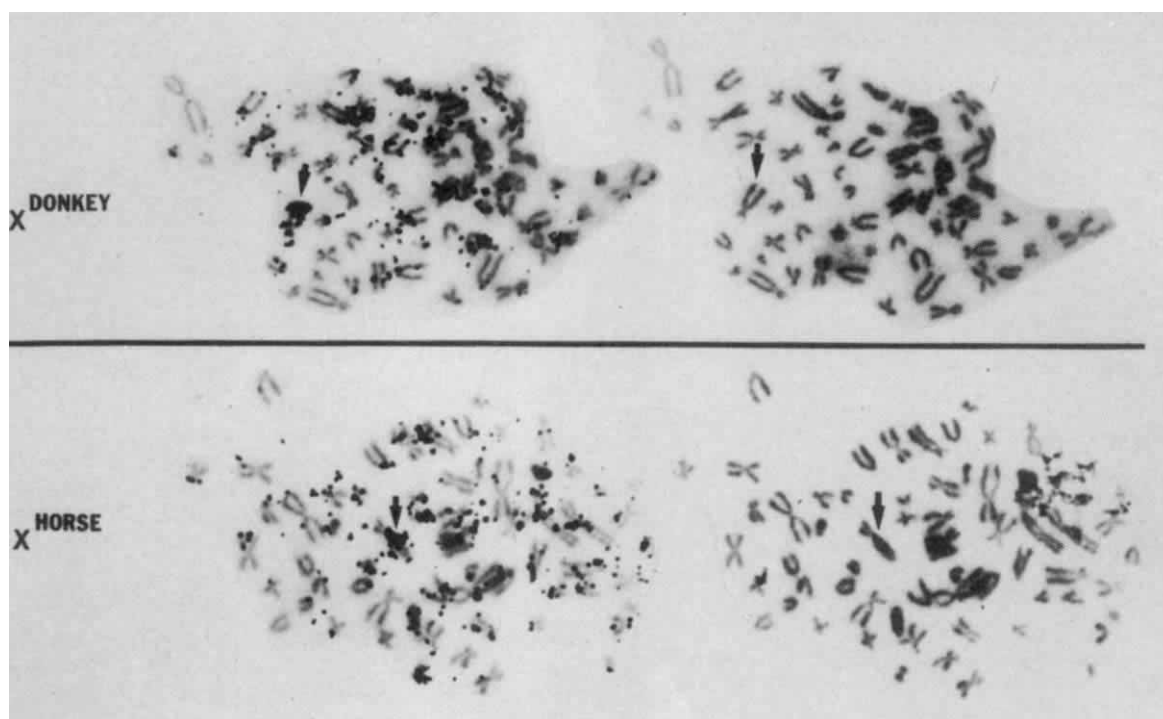


Fig. 1 Autoradiographic patterns showing late replication of the donkey *X* chromosome in clone 267/C3 (upper half) and of the horse *X* chromosome in clone A36-/C4 (lower half).

100% of the total enzyme activity. The remaining five clones yielded opposite results. Figs. 1 and 2 show the late *X* chromosome replication and the electrophoretic patterns of some representative samples, respectively.

These data, while reinforcing the correlation between late DNA replication and genetic inactivity⁶, fully support the clonal evolution concept of the Lyon hypothesis⁵. In a much larger series of clones, Hamerton *et al.*⁹ have obtained similar qualitative results; they have not yet presented confirmatory cytological data, however.

Table 2 Late Replicating *X* Chromosome and G-6-PD Type in Mixed Populations of Female Mule Cells: Effect of Culture Time

Skin fibroblasts (Animal-passage No.)	Late-replicating <i>X</i> ^D No. of cells*	%	Horse-type G-6-PD % of total†
251-7	88 (141)	62.4	59.4 ± 4.2
251-18	89 (113)	78.8	74.3 ± 2.7
251-22	92 (110)	83.6	78.0 ± 1.4
252-7	111 (136)	81.6	78.4 ± 5.2
252-15	98 (115)	85.2	80.2 ± 6.2
252-20	67 (67)	100.0	96.5 ± 0.5
267-7	105 (115)	91.3	90.8 ± 3.4
267-14	93 (93)	100.0	100.0 ± 3.6
WBC			
A36 (8/5/70)	30 (43)	69.8	67.9 ± 1.7
A36 (5/18/71)	—	—	65.1 ± 0.7

* In parentheses the number of cells analysed.

† ± Standard deviation.

The possible existence of selection forces acting *in vitro*⁶ was demonstrated by repeated quantitative assays of the relative activity of G-6-PD types and simultaneous determination of late *X* chromosome replication patterns in three female mule fibroblast lines. A change in the percentage of cells showing a late replicating donkey or horse *X* chromosome took place within a 9-month period (approximately twenty passages). A simultaneous shift in the relative proportion of horse and donkey-type G-6-PD activity also occurred. (Table 2, Fig. 3). The relative G-6-PD activities of leucocytes *in vivo* did not change appreciably over the same time span. In all

three fibroblast lines studied, the rate of adaptation was approximately 1% per passage.

These observations directly indicate that strong selection processes favour those cells in which the horse *X* chromosome is metabolically active. Thus, different conclusions as to the randomness of *X* inactivation would be reached by examining even the same culture at different times.

The contribution of sampling bias to an apparent "non-random inactivation" of the *X* chromosome⁶ was also investigated by studying two skin biopsies approximately 2.5 cm from one another (A36-1, A36-2). Each biopsy (about 0.2 cm²) was cut into halves, one of which was examined directly for G-6-PD types, while the other was again cut in two and established separately in culture. At passage 3 or 4, a sample from the cultured half of each biopsy was examined for both *X* chromosome replication and G-6-PD type and relative activity. At the same time, examinations were also made on cultures derived from the individual quadrants of biopsy A36-2 (A36-2a, 2b). The two biopsies from animal A36 had a significantly different relative proportion of horse-type G-6-PD ($P < 0.005$),



Fig. 2 Cellulose acetate gel electrophoresis of fibroblast lysates after specific staining for G-6-PD. Left to right: mule No. 251, horse, clone A36/C9, clone 252/C2, donkey, mule No. 252. Note absence of donkey-type G-6-PD band in mule No. 252 due to selection *in vitro* (see text).

as did the individual halves of each biopsy (36-1: $P < 0.05$; 36-2: $P < 0.005$). Thus, different results bearing on the randomness of inactivation would have been obtained if the opposite halves of each biopsy had been cultured, or even if the specimen had been cut along a different axis. With such a short period in culture, selection *in vitro* cannot explain these significant differences. Moreover, in biopsy 36-1, the proportion of horse-type G-6-PD was lower in the cultured half of the specimen, the reverse of that expected from the observation on the other mixed cultures (Table 3, Fig. 3).

Table 3 Late Replicating X Chromosome and G-6-PD Type in Two Contiguous Biopsies obtained from the Same Animal

Sample	Late-replicating X^D No. of cells *	%	Horse-type G-6-PD % of total †
A36-1 (skin)	—	—	84.5 ± 0.5
A36-1	46 (67)	68.7	72.9 ± 1.2
A36-2 (skin)	—	—	41.8 ± 1.1
A36-2	35 (54)	64.8	69.7 ± 1.3
A36-2a	54 (76)	71.1	74.9 ± 2.6
A36-2b	49 (66)	74.2	72.7 ± 0.1

* In parentheses the number of cells analysed.

† $\pm$ Standard deviation.

Our data suggest that the female mule skin is composed of irregularly shaped and/or distributed patches of cells of similar G-6-PD phenotype, not necessarily consisting of single clones (Fig. 4). According to this model, the variance among small biopsies would be much greater than that among larger samples of skin. This may explain the different results obtained by various investigators studying mule skin fibroblasts^{6,9-12}. Furthermore, the cell populations from adult animals are far removed in time from X chromosome inactivation during embryogenesis, and the influence of selection forces *in vivo* before culture *in vitro* is difficult to assess.

We have no compelling evidence that selection forces of the same nature as those operating *in vitro* are also active *in vivo*. In man, selection *in vitro* against cells of G-6-PD types A and B^{Mediterranean} has been reported¹³, but there is no evidence of such a phenomenon *in vivo*. Apparent selection *in vivo* against blood cells of G-6-PD type A, deficient in hypo-

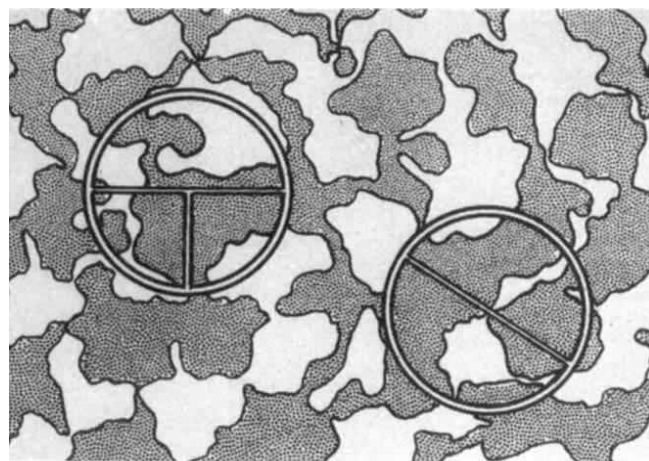


Fig. 4 Distribution of horse and donkey-type cells in female mule skin. Darker areas represent regions of horse-type cells. The segmented circles represent biopsies A36-1 (right) and A36-2 (left). (See text for details.)

xanthine-guanine phosphoribosyl transferase (HGPRT), has been found in doubly heterozygous females¹⁴, while absence of such selection in hair follicles of the same subjects¹⁵ and absence of a selective disadvantage for HGPRT-deficient fibroblasts *in vitro*¹⁶ have been reported. In the female mule, however, the variable expression of G-6-PD phenotypes in different tissues and organs may reflect selection *in vivo*¹⁷. It is likely that selection is related to many genes on the metabolically active X chromosome and selection forces differ in various tissues. This concept may reconcile the discrepancies mentioned above and may possibly be extended to explain the apparent non-random X chromosome expression observed in marsupials¹⁸⁻²⁰. Thus, the female mule fibroblast model provides direct proof of genetic inactivation at the G-6-PD locus coincident with late DNA replication of a given X chromosome, and of maintenance of this inactivation in the progeny of each cell. Experimental models using embryos at early stages of development, in which the influence of *in vivo* selection forces would be minimized, must be employed to answer the question of randomness of X chromosome inactivation.

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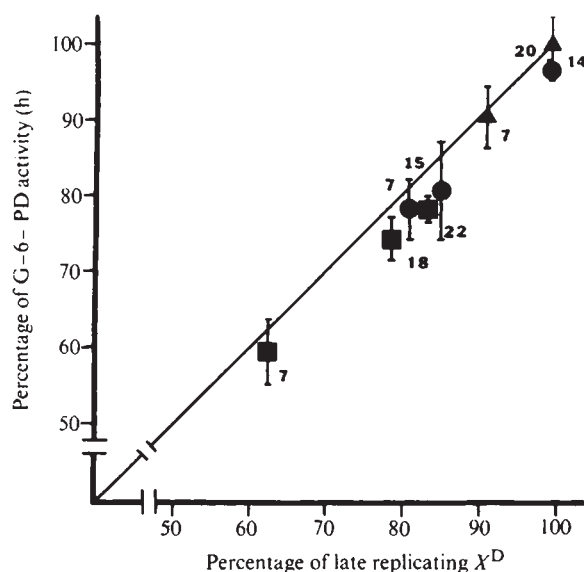


Fig. 3 Effect of culture time on percentages of donkey X chromosome late replication and horse-type G-6-PD activity in cultures of female mule fibroblasts. Passage number for each culture examined is indicated. The line represents perfect correlation ($r=1$); calculated correlation coefficient for these data: $r > 0.95$. ■, 251; ●, 252; ▲, 267.

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Table 1 Autoradiographic Data from Clones derived from Animal No. 202

Clone No.	Gd type	Total cells scored	Cells with DLX	% cells with DLX ^D	% cells with DLX ^H
136	H	148	47	100	—
149	D	159	51	—	100
150	H	167	51	100	—
156	H	139	45	100	—
170	D	151	43	—	100
171	D	148	30	—	100
172	H	154	44	100	—
175	D	166	50	—	100
180	H	148	49	100	—

H, horse. D, donkey.

with hypotonic Hank's solution and air dried slides were prepared, stained with orcein and between 130 and 170 complete and suitably spread metaphase plates photographed. Autoradiographs were prepared by standard methods using Ilford liquid emulsion (K2 type) and exposed for 9 days. The cells which had been previously photographed were relocated and examined for a differentially labelled *X* chromosome (DLX), defined as a medium-sized chromosome which had at least twice as many autoradiographic grains as any other chromosome of similar size² (Fig. 1). Five of the nine clones typed *Gd^H*, and in each of these 100% of cells with a DLX showed a DLX^P, and conversely in the four clones which

G6PD Expression and *X* Chromosome Late Replication in Fibroblast Clones from a Female Mule

THE relationship between late DNA replication and *X* chromosome inactivation is supported by strong circumstantial evidence¹⁻³. The use of clones derived from a female mule¹ typed for *Gd* and at the same passage labelled with ³H-TdR and subsequently autoradiographed should provide final proof of this relationship.

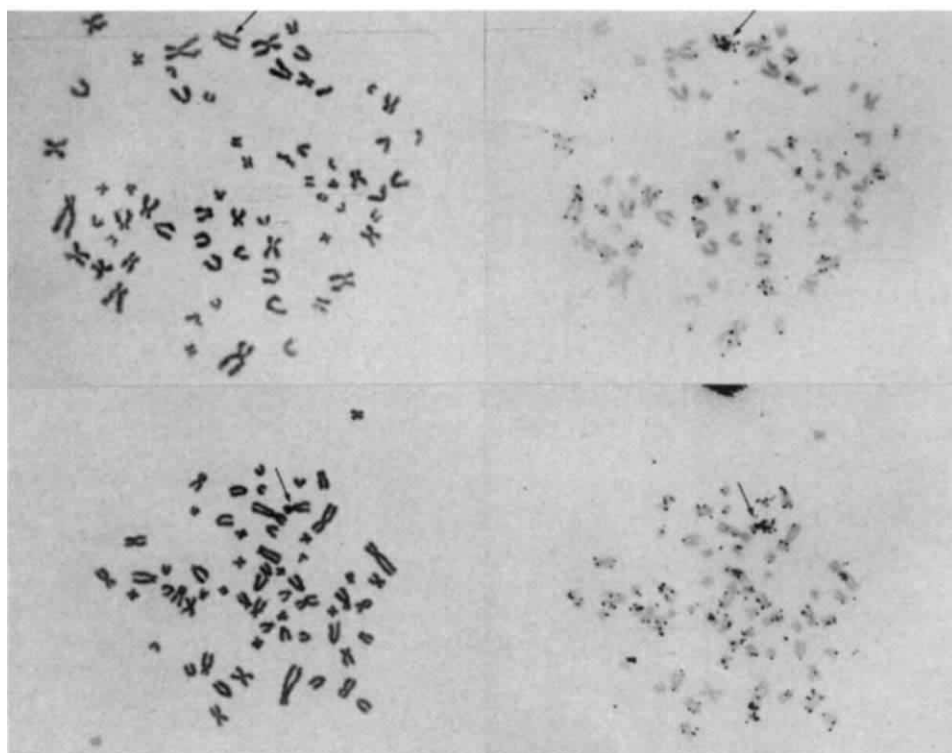


Fig. 1 Autoradiographic patterns illustrating late replication of the donkey (top) and horse (bottom) *X* chromosomes.

Nine clones derived from a fibroblast culture from animal No. 202 (mule) were typed for *Gd* by one of us (B. J. R.)¹. Cultures from these clones were treated with ³H-TdR (specific activity, 1.9 Ci/mmol; Schwarz BioResearch Inc.) by M. R., who was unaware of the *Gd* typings. ³H-TdR was added to the culture medium at a final concentration of 1 μ Ci/ml. for 5 h before collection. Colcemid was added 3 h before termination of the cultures by trypsinizing; they were then treated

typed *Gd^P*, 100% of cells with a DLX showed a DLX^H (Table 1).

We conclude, from the absolute correlation observed between the autoradiographic and the genetic data presented here for nine fibroblast clones derived from a female mule, that late replication of one *X* chromosome is the cytological manifestation of genetic inactivity.

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Normal Progeny from Fertilization *in vitro* of Mouse Oocytes matured in Culture and Spermatozoa capacitated *in vitro*

ALTHOUGH primary mammalian oocytes have the capacity for maturation¹⁻⁷ and fertilization^{8,9-11} *in vitro*, viable foetuses have not been obtained in such studies^{8,11}. Conversely, fertilization *in vitro* of mature tubal mouse oocytes with capacitated sperm, recovered from the uterus, led to blastocysts in culture which developed into normal, fertile offspring subsequent to implantation into suitable recipients^{12,13}. More recently, 15-day-old foetuses were obtained after fertilization *in vitro* of mouse oocytes matured in culture by sperm capacitated in the uterus followed by implantation of blastocysts¹⁴. We have now ob-

tained normal progeny after implantation of embryos obtained from oocyte maturation as well as sperm capacitation *in vitro*.

Between thirty and fifty immature oocytes, with a well defined germinal vesicle (Fig. 1A), were obtained from each 6-8-week-old virgin mouse (ICR/Ha or C57BL/6J strains) by teasing of ovarian follicles in a 1:1 mixture of normal saline and Ham's F-10 tissue culture medium at pH 7.0. The oocytes were separated from cellular debris and cultured for 8-10 h in a drop of Ham's F-10 or modified Whitten and Bigger's medium (sodium pyruvate 0.60 mM instead of 0.33 mM) in a 60 mm plastic Petri dish under oil at 37° C in 5% CO₂ in air. Epididymal spermatozoa from proven fertile males were capacitated *in vitro* by incubation in heat inactivated human follicular fluid and human tubal fluid (1:2) at 37° C for 4 h¹⁵.

Approximately 1×10^8 capacitated spermatozoa (0.3 ml.) was added to a Petri dish containing fifty oocytes matured *in vitro* which were suspended in two drops of F-10 medium. The mixture of eggs and sperm was completely covered with a layer of paraffin oil (Fisher Scientific viscosity 125/135). The Petri dish was incubated at 37° C in 5% CO₂ in air. After 24 h, the two-cell embryos were transferred to fresh medium and in 3 days developed to the blastocyst stage. The blastocysts were then transplanted to recipient mothers as described before¹³ and birth occurred 17-18 days after transplantation. Including the 4 days of growth *in vitro*, the total gestation period was 21-22 days.

Of 325 oocytes cultured (Fig. 1A), 195 (60%) shed the first polar body (Fig. 1B); this was the criterion for maturation. Fertilization *in vitro* of 140 oocytes was attempted, yielding thirty-two (22.8%) apparently normal two-cell embryos. Eleven (34.3%) embryos developed to blastocysts (Fig. 1C and D) and their transplantation to surrogate mothers resulted in five normal progeny (three female, two male) which were subsequently found to be fertile. Although the rate of fertilization and development of embryos *in vitro* was low, this experiment indicates that normal fertile progeny can develop entirely *in vitro*. Better yields will result as the technique is developed further.

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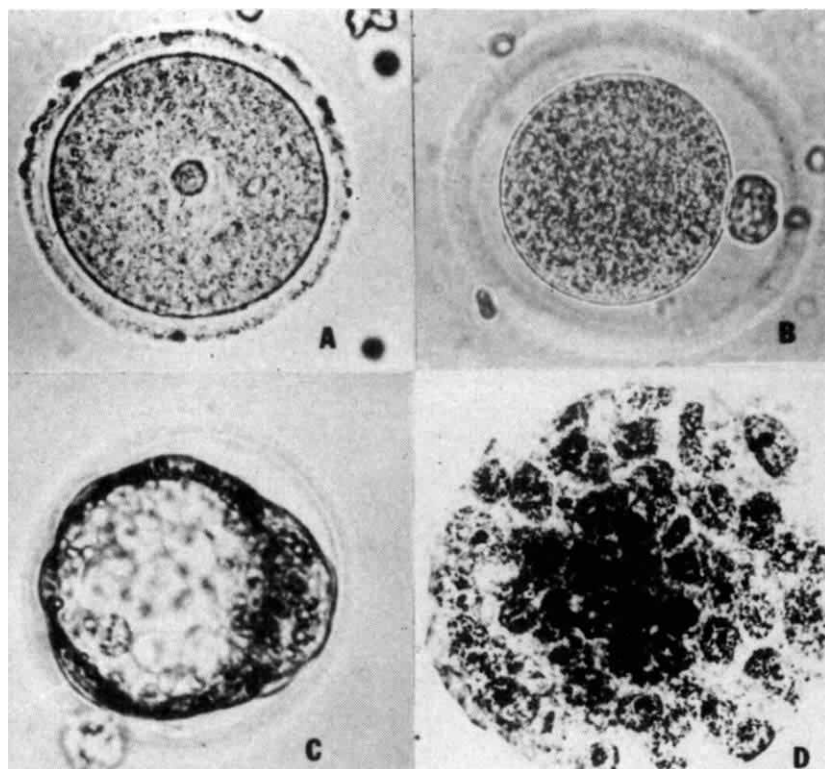


Fig. 1 Development of blastocyst for ovarian oocyte. A, Immature ovarian oocyte with well developed germinal vesicle. B, Mature oocyte, note the first polar body. C, Living blastocyst. D, Fixed blastocyst.

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Acute Effect of a Glucocorticoid on Normal Human Sleep

ELECTROENCEPHALOGRAPHIC studies of sleep suggest that the magnitude of sleep disturbances in depressed and schizophrenic subjects varies with the degree of psychic turmoil¹⁻⁶. Psychoendocrine studies of psychiatric patients have suggested that adrenal cortical steroid excretion is elevated with subjective distress⁷⁻¹³. Some endocrine studies have shown that nocturnal secretion of adrenal cortical steroids is elevated at least part of the time in psychiatric patients¹⁴⁻¹⁷. We have undertaken to determine the effect of a glucocorticoid on normal human sleep.

The subjects were twelve healthy students, six males and six females, aged 18-22, who were living for a period of months as normal volunteers on a research ward at the Clinical Center, the National Institutes of Health. The subjects went to bed each night at 2330 and were woken at 0730. During sleep, continuous recordings of the electroencephalogram, electro-oculogram and electromyogram were obtained. Nap-

ping was prohibited. Each night 6 h before retiring, the subjects received the same number of identical capsules; drugs were given with dinner to minimize gastric irritation. Prednisone, a synthetic glucocorticoid steroid possessing about four times the equivalent mg potency of cortisol¹⁸, was given to half the subjects in a dose of 5 mg and half the subjects in a dose of 60 mg in the following schedule: after two or more nights of conditioning to the sleep recording, a baseline (placebo) period of three nights, drug night No. 1 (D₁), placebo night (P), drug night No. 2 (D₂) and a 3-day recovery (placebo) period (R₁, R₂, R₃). In addition, three of the subjects were studied at a dose of 20 mg, given once only following two nights baseline, with one recovery night following the drug night. The sleep records were evaluated without knowledge of the drug status according to standard methods¹⁹. The data for 5 mg and 60 mg doses were analysed by multifactorial analysis having repeated measures on the same elements²⁰. Statistical difference between individual drug nights and the baseline period was tested with the contrast of means procedure. The Friedman analysis of variance²¹ was used to test the data for latency to the first rapid eye movement sleep period since the assumption of homogeneity of parts was not met (*F* max test)²⁰.

The highest dose tested, 60 mg of prednisone, led to highly significant reduction in rapid eye movement (REM) sleep, an increase in stage II sleep, and an increase in time to the onset of the first REM period of the night, the REM latency (RL) (Table 1). All subjects responded in the same way. At the lower two doses, 5 mg and 20 mg, similar trends were seen with regard to REM and REM%, but these did not reach the *P* < 0.05 level of significance. We feel the results of 20 mg reflect the small number of subjects tested; preliminary evidence from an ongoing study we are conducting with psychiatric patients also suggests that REM sleep is reduced at this dosage. No changes in sleep latency, early morning waking, eye movement activity in REM, or the ratio of stage III to stage IV were noted. The subjects were apparently unaware of when the drug was given; their guessing correctly was no better than chance.

Based on the change in each individual while on the medication, the average % change from baseline REM and non-REM sleep (NREM) for each of the three doses is shown graphically in Fig. 1. Over this dose range, there seems to be a fairly clear dose response effect. Using the least squares technique, the effect of varying doses of prednisone on REM sleep is described by the regression equation $Y = 9.78 - 0.56 X$ (slope differs from zero, *P* < 0.005). The effect on NREM sleep is described by $Y = 0.11 + 0.22 X$ (slope differs from zero, *P* < 0.01).

We did not find some of the sleep changes typically associated

Table 1 Effect of Prednisone, Three Different Doses, on Normal Human Sleep

Dose	No. of subjects	Baseline	D ₁	P	D ₂	R ₁	R ₂	R ₃	
5 mg	6	RL	92±23	108±42	98±36	98±22	94+55	85±21	86±45
		REM	98±16	88±24	95±17	87±19	109±19	102±26	97±30
		II	259±28	282±42	232±26	235±20	249±32	256±34	244±43
		Delta	61±17	68±30	70±26	72±18	64±20	58±10	57±15
		Int. A	7±14	10±9	5±7	12±27	9±9	6±10	7±15
20 mg	3	RL	109±36	85±18	78±20				
		REM	118±20	83±6	121±6				
		II	250±16	283±6	223±45				
		Delta	68±12	63±18	86±20				
		Int. A	1±1	1±1	0				
60 mg	6	RL*	70±14	89±12	76±23	81±12	64±14	67±10	64±10
		REM†	105±8	60±12‡	131±21	60±13‡	116±7	117±7	118±11
		II§	251±14	300±37	258±20	277±22	243±23	229±30	258±74
		Delta	63±31	68±23	63±26	72±31	64±31	75±30	58±18
		Int. A	3±2	4±4	2±2	8±7	2±3	3±3	4±5

Mean ± s.d. (min). * Friedman's analysis of variance, $\chi^2 = 18.85$, *P* < 0.01. † *F* = 18.25, *P* < 0.005. ‡ *F* = 70.75, *P* < 0.0005. § *F* = 5.25, *P* < 0.05. || *F* = 16.22, *P* < 0.005. (Conservative degrees of freedom = 1, 10.)

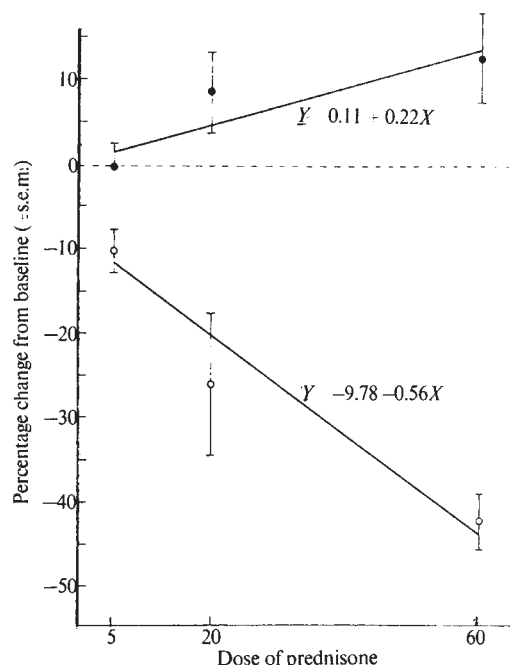


Fig. 1 The effect of prednisone on normal human sleep. ●, Non-REM; ○, REM.

with psychic stress, such as increased time to fall asleep, early morning insomnia, or decreased stage III and IV (delta) sleep¹⁻⁶. There was a trend, however, towards increased intermittent wakefulness (Int. A., the amount of wakefulness between the beginning and end of sleep) during the night on the drug days, though it was not statistically significant (Table 1). Whether or not alterations in REM sleep are correlated with changes in endogenous steroid secretion must await further data, both from normals and psychiatric patients. It cannot be assumed that a single oral dose mimics endogenous secretion of steroids during stress.

It seems that the REM suppressive effects of prednisone are relatively long lasting. During the last 2 h of the night, a period beginning 12 h following the ingestion of the drug, REM sleep was still reduced (27 min versus 43 min during the baseline period, $P < 0.01$, for the 60 mg dosage).

The results we obtained are not consistent with previous studies on rabbits and cats which were given exogenous glucocorticoid steroids without effect on sleep^{22,23}; either species differences or the particular steroid given may be important. Moreover, the effect we obtained may be only an acute one: a previous study showed no difference in sleep patterns between asthmatic patients chronically receiving prednisone and those not receiving it²⁴.

The results obtained, however, do provide another quantifiable measure of steroid effects on the activity of the human central nervous system, although the mechanism of action is not known. Research on the biochemical control mechanisms of sleep has focused on brain amines^{25,26}, which are known to be affected directly and indirectly by adrenal cortical steroids²⁷⁻²⁹. Glucocorticoids are also thought to alter brain excitability by their influence on electrolytes³⁰. However steroids act, the data presented here suggest an indirect mechanism. The plasma half life of prednisone is 60 min¹⁸, which implies that the REM suppression effect is strongly present long after circulating prednisone has presumably disappeared.

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Increased Hepatic Microsomal Enzyme Activity from Occupational Exposure to Certain Organochlorine Pesticides

THERE is increasing concern about the possible harmful effects resulting from accumulation of organochlorine pesticides in soil, water and in the food of animals and man. DDT, the first organochlorine pesticide (introduced in 1941), has been supplemented by the cyclodiene group, which includes aldrin, dieldrin and endrin*. These compounds, like DDT, accumulate in fat and are only excreted slowly. Their toxic effects are also similar, large doses causing convulsions and

* Dieldrin contains not less than 85% HEOD, which is 1, 2, 3, 4, 10, 10, hexachloro-6, 7, epoxy 1, 4, 4a, 5, 6, 7, 8, 8a, octahydro-endo 1, 4, exo 5, 8, dimethanonaphthalene. Aldrin contains 95% HHDN, which is 1, 2, 3, 4, 10, 10, hexachloro-1, 4, 4a, 5, 8, 8a, hexahydro-endo 1, 4, exo 5, 8, dimethanonaphthalene. Endrin as sold contains 92% of the endo-endo-isomer of HEOD.

hepatic damage. The blood concentrations currently found in the general population of Europe are unlikely to be directly toxic, although present levels of environmental exposure have been claimed to be harmful to fish¹ and predatory birds². Doses of these pesticides below those at which direct toxic effects are observed have, however, been shown to induce hepatic microsomal enzymes in animals³, and in the rat this occurs with as little as 10 p.p.m. of DDT in the body fat⁴. Whether current levels of environmental exposure to organochlorine pesticides are sufficient to produce enzyme induction in man is uncertain: Kolmodin *et al.*⁵ found a decrease in the half life of injected antipyrine in the plasma of men manufacturing pesticides, and Poland *et al.*⁶ reported changes in cortisol and phenylbutazone metabolism in factory workers with heavy exposure to DDT. In studies of workers engaged in the manufacture of pesticides, hepatic microsomal enzyme activity was assessed from changes in the urinary excretion of D-glucaric acid (an end product of the glucuronic acid pathway of the liver⁷) and related to blood pesticide levels.

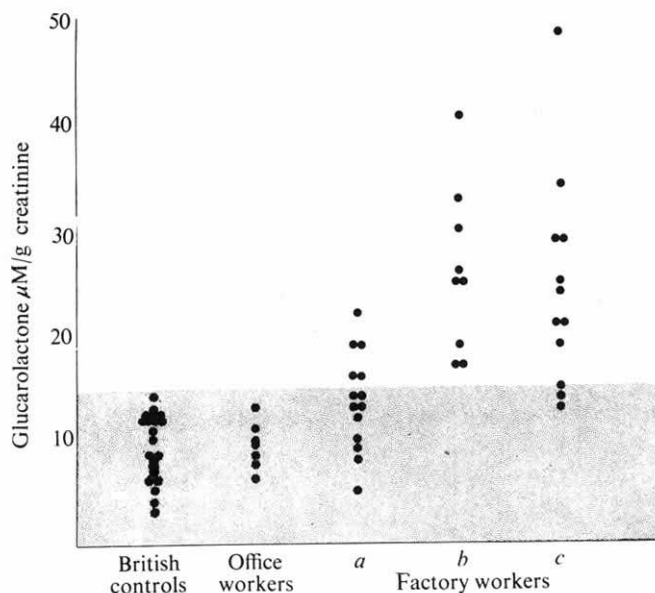


Fig. 1 D-Glucaric acid excretion in various groups of employees. The tinted area indicates the range found in control subjects. a, Aldrin/dieldrin; b, endrin; c, Aldrin/dieldrin/endrin.

Employees in the factory at Rotterdam work eight-hour shifts. An aliquot from the total urine collected during that time was frozen and maintained at -20°C for transport to England. The concentration of D-glucaric acid was measured from the inhibitory effect of glucarolactone, to which it is converted by heating at pH 2, on β -glucuronidase⁸. The results were expressed as μmol glucarolactone/g creatinine, which we have found in a previous study to correlate closely with the total daily excretion.

Of the forty-six samples received from the factory, seven were from office staff who had never been directly exposed to pesticides, the offices being situated one kilometre from the production area. None had an increased excretion of D-glucaric acid, concentrations being very similar to those in twenty-one control subjects in Britain (Fig. 1). Five of the fourteen men employed in an area of the plant where Aldrin and dieldrin alone are produced had concentrations above the normal upper limit, but none were markedly increased; the difference between the values for this group and those of the controls was not statistically significant ($P > 0.05$ Wilcoxon's rank test). Men employed in the manufacture of endrin alone had the

greatest D-glucaric acid excretions. Nine of the thirteen examined had values above normal, and the excretion of the group was significantly greater than of the controls ($P < 0.01$). Four men with normal values had worked with endrin for less than 4 months. The remaining group of workers examined comprised twelve men who were working in both plants, with exposure to Aldrin, dieldrin and endrin. In nine of them increased D-glucaric excretion was found, and the values were similar to those found in the workers who had been exposed to endrin alone. Blood pesticide levels were measured by gas-liquid chromatography with electron capture¹⁰. This technique is equally sensitive for dieldrin (measured as HEOD) and endrin, and since Aldrin is rapidly epoxidized in the body to dieldrin, the blood HEOD level can also be used to measure exposure to Aldrin. Blood HEOD values ranged from 0.0005 $\mu\text{g}/\text{ml}$. to 0.110 $\mu\text{g}/\text{ml}$., with a mean of 0.026 $\mu\text{g}/\text{ml}$. No correlation with D-glucaric acid excretion could be detected. Blood levels of *pp'*DDE (the major metabolite of *pp'*DDT) ranged from 0.0005 $\mu\text{g}/\text{ml}$. to 0.042 $\mu\text{g}/\text{ml}$. The levels were lower in endrin workers ($P < 0.01$, Wilcoxon's rank test) and showed a significant inverse correlation with D-glucaric acid excretion ($r = -0.389$; $P < 0.05$). No endrin was detected in the blood.

This study shows that many of the men engaged in the manufacture of endrin have significantly increased activity of hepatic microsomal enzymes, for although the urinary excretion of D-glucaric acid is only an indirect measure of enzyme activity, our studies in man to date indicate that it is both sensitive and quantitative^{8,11}.

Furthermore, in the guinea-pig which, like man, is unable to convert glucuronic acid to ascorbic acid, we found a significant correlation between D-glucaric acid excretion and the total liver content of the microsomal enzyme cytochrome P-450¹¹.

In spite of considerable precautions, nearly 70% of men exposed to Aldrin and dieldrin have increased blood concentrations of HEOD. The mean value of 0.026 $\mu\text{g}/\text{ml}$. is considerably higher than in the population of southern England, which has ranged between 0.0013 in 1966 and 0.0009 $\mu\text{g}/\text{ml}$. in 1968¹². The values are, however, well below the minimum level of HEOD (0.2 $\mu\text{g}/\text{ml}$.) known to be toxic. The relatively small increase in D-glucaric acid excretion, and the lack of correlation with blood concentrations of HEOD found in those producing Aldrin and dieldrin, suggest that the level of exposure in the plant is insufficient to induce hepatic enzymes.

Endrin is used for the control of pests, particularly of cotton and tobacco, and also of maize, sugar cane and fruit trees. It has never been detected in soil or water, and none has been found in food in Britain¹³, and only trace amounts in the United States¹⁴. Our inability to detect endrin in the blood of workers exposed to it is probably due to its rapid metabolism in the body, as in cases of accidental endrin poisoning the blood level has been found to decrease rapidly over a period of hours¹⁵. In areas where it is widely used, it has not been found in the blood of the general population¹⁶. In the rat and the dog, endrin is rapidly converted to a hydrophilic compound, 9-ketoendrin, but so far this compound has not been detected in man. Endrin itself, a metabolite, or even isodrin (the isomer of dieldrin from which endrin is produced), might be the compound responsible for enzyme induction.

The low *pp'*DDE levels found in endrin workers also suggest enzyme induction. Both *pp'*DDT and *pp'*DDE, its main metabolite, are metabolized by microsomal enzymes and *pp'*DDE levels have been reported to be lower in epileptic patients on phenobarbitone or phenytoin than the general population¹⁷. A significant inverse relationship between the blood *pp'*DDE level and urinary D-glucaric acid excretion is further evidence that this is an effect of enzyme induction. Increased urinary concentrations of 6β -hydroxycortisol have also been reported in endrin workers¹⁸, which is probably the result of induction of the hepatic enzyme cortisol 6β -hydroxylase, for this also occurs following administration of drugs such as phenytoin with known inducing properties.

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Strain Differences in Thymus Weight in Mice with Different Predispositions to Spontaneous Mammary Cancer

It has been demonstrated that early thymectomy in high mammary tumour strains of mice results in retarded development of spontaneous mammary tumours¹⁻⁷. We have shown that early thymectomy also inhibits the growth of syngeneic transplantable tumour in the high cancer C3H/He mouse strain⁸, whereas the transplantation of one to four additional syngeneic thymuses stimulates the growth of this tumour⁹. Thus, it appears that the thymus exerts an influence on mammary tumour development in high cancer strains of mice.

We have suggested that the different susceptibility of mouse strains to mammary tumour is related, among other factors, to the hereditarily determined features of the thymus in high cancer strains of mice⁹.

One of the morphological characteristics of the thymus is the weight of this gland. In the work described here, thymus index (the ratio of thymus weight to body weight) was compared in strains of mice varying in their susceptibility to mammary tumour.

Table 1 Tumour Frequency in Inbred Strains of Mice Used¹¹

Strain	Sex	Longevity (days) M ± m	Tumour frequency (%)			
			Mammary gland	Liver	Lungs	Leucosis
AKR	♀♀	298 ± 5.88	—	—	—	91.0
C57BL	♀♀	656 ± 19.80	—	—	—	31.1*
BALB/c	♀♀	417 ± 9.78	1.8†	—	12.2	5.0
C3H/He	♀♀	291 ± 4.69	83.9	—	—	—
A/He	♀♀	484 ± 9.87	57.9	10.8	12.3	12.3

* In C57BL mice leucosis develops at the age of over 600 days.

† In BALB/c mice infected with Bittner virus frequency of mammary tumour increases strikingly.

Table 2 Strain Differences according to Value of Thymus Index

Strain	Females		Males	
	No. of animals	Arbitrary mean of thymus index	No. of animals	Arbitrary mean of thymus index
AKR	174	5.3	38	4.0
Random bred mice (r/b)	145	4.1	84	3.8
C57BL	155	4.2	115	3.6
BALB/c	60	3.6	55	3.2
C3H/He	141	2.6	101	2.4
A/HeJ	149	2.3	66	2.1

Mice were obtained from the colony of the USSR Academy of Sciences "Stolbovaya". The frequency of the tumours in the mouse strains used is shown in Table 1.

The mice were killed with ether and weighed. Thymuses were removed and weighed. Ten to twelve females in each age group, except BALB/c, were studied. In all male age groups and in the female BALB/c group there were four to ten mice. An arbitrary mean thymus index was calculated for each strain by summing the mean value of the thymus index of all the age groups and then dividing the sum by the number of these groups, that is, by 14 in the female and 11 in the male groups.

Paired comparison of the empirical values of thymus index in each age group was used to test the significance of the differences in thymus index between animals of different strains. The difference between these strains was considered to be significant if the member in the middle of the series composed of the differences in the observed values of thymus indices for each age group of a given strain differed significantly from zero.

The results are presented in Figs. 1 and 2 and Table 2. There were differences between the thymus index/age curves of the different strains of mice. In adult AKR female mice the

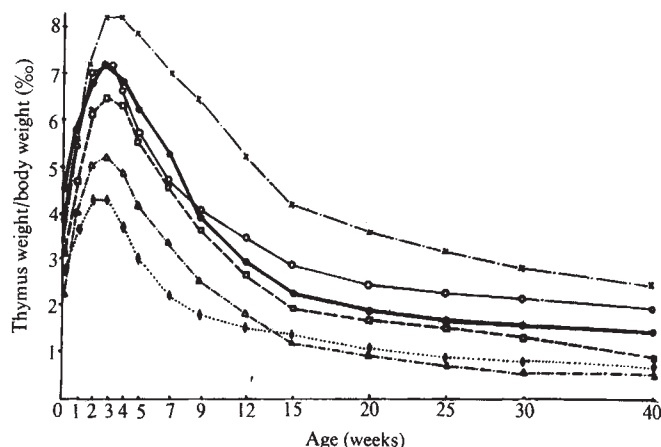


Fig. 1 Weight changes with ageing of the thymus index in mouse strains (females). x, AKR; ●, random bred; ○, C57BL; □, BALB/c; Δ, C3H/He; ◆, A/HeJ.

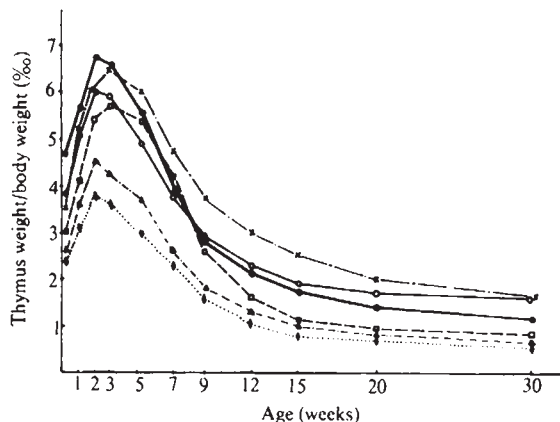


Fig. 2 Weight changes with ageing of the thymus index in mouse strains (males). Symbols as in Fig. 1.

curve of the thymus index lies significantly above the curves of all the other strains and of the random bred animals. This is consistent with Metcalf's¹⁰ data and is related to the predisposition of the animals to leucosis. The curve of the thymus index in the low cancer C57BL mouse strain and in the random bred animals is significantly higher than the curve for the BALB/c strain which has an intermediate predisposition to mammary tumour. The curves of the high cancer C3H/He and A/HeJ strains are lower than the other curves. In males a similar but less clear-cut pattern of strain difference was also observed. The results obtained indicate that high cancer strains of mice have a much smaller thymus index compared with mice in which spontaneous mammary tumours are rare.

The correlation coefficients between the arbitrary mean thymus index and the frequency of spontaneous mammary tumour validate this point ($r = -0.89$, $P = 0.01$). This may be evidence in favour of the suggested genetically determined differences in the specific influence exerted by the thymus on the development of mammary tumours.

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Potential Use of Nitrofurans in Radiotherapy

It has been suggested that the hypoxic centres within a tumour mass are likely to be relatively resistant to sterilization by ionizing radiation¹. Compounds which could be introduced into such hypoxic centres and which can mimic the radiation sensitizing effect of oxygen may therefore be of great value in

the radiation therapy of cancer. A number of chemicals are known to sensitize mammalian cells to the effects of ionizing radiation². One such compound is *para*-nitroacetophenone (PNAP), which was selected as a potential radiosensitizer because of its strong electron affinity³. Subsequent studies demonstrated that PNAP was a good selective hypoxic radiosensitizer in mammalian cells^{4,5}. Recent studies with analogues of PNAP indicate that the nitro group is essential for radiosensitizing activity in Chinese hamster cells, and furthermore that sensitizing ability improves with increasing electronegativity (manuscript in preparation). Because 5-nitrofurans are known to be more electronegative than the corresponding nitrobenzene derivatives⁶, we tested two well documented nitrobenzene derivatives for radiosensitizing activity.

Sensitization studies were performed with asynchronous Chinese hamster cells using cell culturing techniques and irradiation procedures as described previously⁴. Fig. 1 shows the effect of 500 μ M 5-nitro-2-furaldehyde-semicarbazone (nitrofurazone, Norwich Pharmacal, Norwich, New York) on the survival of Chinese hamster cells irradiated in air and in hypoxic conditions. The drug was placed on the cells in complete medium before irradiation and was in contact with the cells throughout the duration of the irradiation. It is apparent that nitrofurazone strongly sensitizes hypoxic hamster cells whereas in air there is a slight degree of protection. Cells exposed to 500 μ M nitrofurazone for an equal time without irradiation lost no plating efficiency due to the drug alone. Using the relation previously described⁴, an enhancement ratio (ER) of ~ 2.0 for 500 μ M nitrofurazone in hypoxia was calculated. To determine whether this radiosensitizing effect was unique to nitrofurazone, we tested N-(5-nitro-2-furfurylidene)-1-aminohydantoin (nitrofurantoin, Norwich Pharmacal, New York) for radiosensitizing ability. Fig. 2 shows survival curves for Chinese hamster cells irradiated in air and in hypoxia in the presence and absence of 500 μ M nitrofurantoin. An enhancement ratio of ~ 1.7 was obtained for the selective hypoxic radiosensitizing effect. The same concentration of nitrofurantoin had no effect on the plating efficiency of non-irradiated cells.

Recent studies on the mode of action of nitrofurans derivatives indicate that these compounds can be "activated" by reductive metabolism to give rise to reduction intermediates which are toxic to cells^{7,8}, bind irreversibly to proteins⁷, and cause single strand breaks in bacterial DNA⁹. Irradiation of aqueous

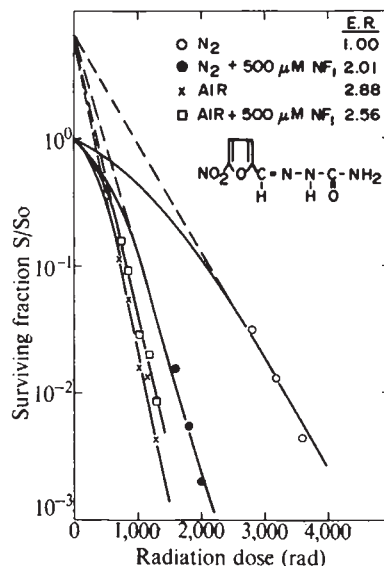


Fig. 1 Survival curves for Chinese hamster cells irradiated with 250 kVp X-rays in air saturated conditions ($\times$), in air saturated conditions with 500 μ M nitrofurazone ($\square$), in hypoxic conditions ($\circ$), and in hypoxic conditions with 500 μ M nitrofurazone ($\bullet$).

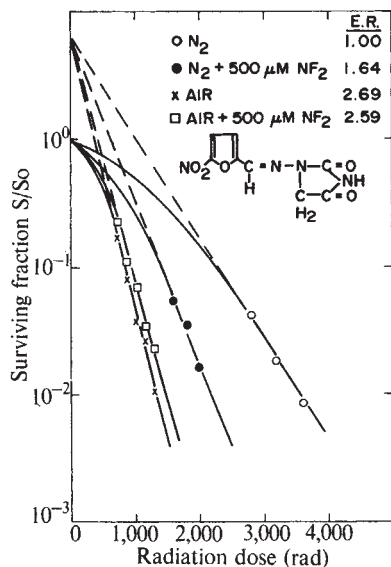


Fig. 2 Survival curves for Chinese hamster cells irradiated with 250 kVp X-rays in air saturated conditions (×), in air saturated conditions with 500 μM nitrofurantoin (□), in hypoxic conditions (○), and in hypoxic conditions with 500 μM nitrofurantoin (●).

solutions of nitrofurantoin may also result in partial reduction of the nitrofurantoin by means of the hydrated electrons produced by radiolysis of water¹⁰. Such reduction intermediates of the nitrofurantoin produced by ionizing radiation may be short-lived free radical species. Solutions of nitrofurantoin or nitrofurantoin (both at 500 μM) irradiated in hypoxia in complete medium and placed quickly (within 1 min) on Chinese hamster cells showed no increased toxicity as compared with cells exposed to the unirradiated drug solution. This result suggests that hypoxic radiosensitization is being effected by a short-lived product as opposed to a stable product.

The data presented here show that nitrofurantoin derivatives are excellent radiosensitizers in hypoxic mammalian cells in concentrations displaying no acute toxicity *in vitro*. These compounds have already found wide clinical application and accept-

ance as antibacterial agents¹¹, and the toxicological and pharmacological properties have been well established, so there is good reason to test 5-nitrofurantoin derivatives as radiation sensitizers in experimental tumour systems as well as human cancers.

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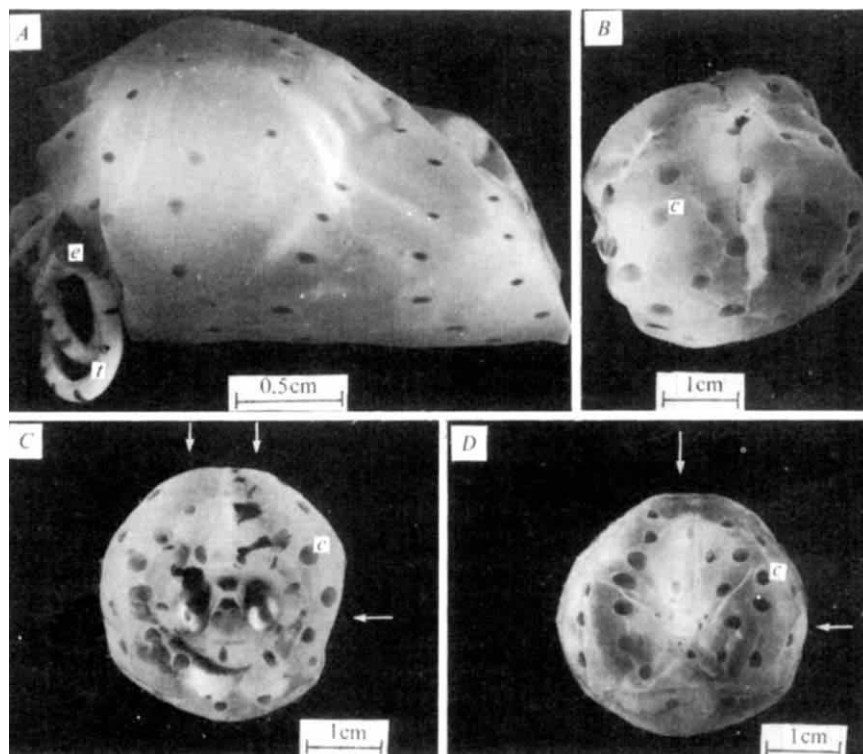
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Taonius megalops, a Squid that Rolls Up into a Ball

THERE are few recorded observations of living oceanic squids, but during a recent North Atlantic cruise, undamaged live branchioid squids were caught. In life, *Taonius megalops* are

Fig. 1 A, Lateral view of *Taonius* showing the first stage in the balling up sequence. The fin has become inverted into the mantle. B, Side view of a balled up *Taonius megalops*. The head and the fin are no longer visible. The head has been withdrawn into the mantle cavity and the fin has been enclosed in a folding of the mantle. C, Anterior view, showing the head completely obscured within the mantle; the eyes are disguised by the concentric arrangement of chromatophores. The black areas in the animal are patches of ink that have been discharged into the mantle cavity. The arrows indicate the position of the eyes. D, Posterior view showing the folded and withdrawn fin surrounded by the mantle. The chromatophores lie concentrically. The arrows indicate the position of the tail fin. c, Chromatophore; e, eye; t, tentacle.



transparent except for deeply pigmented eyes, a silvery ink sac and chromatophores which are sparsely distributed over the mantle surface. In undisturbed specimens these chromatophores are contracted to tiny points, but when the squid is disturbed the chromatophores dilate and increase in area about four times, still widely separated (Fig. 1). The remainder of the animal remains transparent.

Severe stimuli produce inking; the squid ejects ink into the water, and darts away from the ink cloud. Further chasing of the squid or attempts to lift it from the water produce a balling response in which the animal rolls itself into a sphere, retracting the tail and head into the mantle. This process occurs in distinct phases. First, the tail fin and pen are inverted into the mantle (Fig. 1 A, D). The process stops at this stage if the irritation is withdrawn, and after several minutes the tail will evert back to its usual position. If the stimuli continue, the head and tentacles are withdrawn into the mantle cavity and the cavity becomes filled with seawater. The whole animal becomes a turgid sphere with the two long arms extending from it. If the stimulus continues, the two arms withdraw into the mantle. In the spherical squid the expanded chromatophores lie in a series of points on concentric circles (Fig. 1 B, C, D). This pattern obscures the nature of the eyes and the tail fin. Continuing stimuli to the balled up *Taonius* causes it to ink, but the ink is not released and it fills the mantle cavity. The animal then becomes visible as a spherical black ball.

Recovery of normal shape from this stage takes about half an hour. It starts with the extending of the head and tentacles, followed by the pen and tail, and only after the squid has been swimming undisturbed for several minutes does it begin to release ink. These considerable distortions in shape and of the relative position of parts within the animal take place without any apparent damage.

Inking and chromatophore displays are well known in cephalopods but balling up has not been described before. Such behaviour is probably of survival value to *Taonius megalops*, and it is interesting to speculate how many other squid only known from preserved specimens would exhibit similar, or even more bizarre, behaviour if observed live.

I thank Professor J. Z. Young, the National Institute of Oceanography and Mr P. David for allowing me to join their biological cruise. Mr R. Aldrid helped considerably aboard ship. The US National Geographic Society gave a grant towards the photographic equipment used in this and other studies of live cephalopods.

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Smell and Foraging in Shearwaters and Petrels

BIRDS of the order Procellariiformes (the tube-nosed swimmers: albatrosses, shearwaters and petrels) are unusual in the development of their olfactory equipment, and some authors have suggested that these pelagic birds locate food by smell¹⁻³. I report here positive responses from shearwaters and petrels to airborne odour trails controlled for visual cues.

During the summer of 1970 I tested the olfactory responses of the great shearwater (*Puffinus gravis*), sooty shearwater (*P. griseus*), Leach's petrel (*Oceanodroma leucorhoa*) and Wilson's petrel (*Oceanites oceanicus*), at the mouth of the Bay of Fundy. I anchored my boat at slack tide, and began

odour trail tests with identical sponges soaked in cod liver oil or seawater (control) and placed on top of poles mounted vertically on inflated 0.8 m diameter inner tubes. Each sponge was positioned 1 m above the ocean surface 50 m astern of the boat, having been carried there by the current and restrained by a line. Sponges were presented singly to the birds for 15 min, in sequences of randomly ordered pairs, with inter-trial periods of 5-10 min.

The number of upwind flights passing within an estimated 5 m on either side of the sponge was tallied for each species during a trial period. In the absence of oil slicks and with virtually indistinguishable stimuli, I concluded that the airborne odour trail of cod liver oil was the only factor by which the two sponges could be distinguished.

Table 1 Petrel and Shearwater Flights to Water-soaked and Cod Liver Oil-soaked Sponges during Daylight

Date	Onset of trial	Wilson's petrel		Leach's petrel		Great shearwater		Sooty shearwater	
		OS	WS	OS	WS	OS	WS	OS	WS
July 7	1505	43	—	0	—	0	—	1	—
	1525	—	14	—	0	—	0	—	0
	1550	—	16	—	0	—	3	—	3
	1617	38	—	0	—	5	—	4	—
July 22	1420	—	3	—	0	—	0	—	9
	1443	14	—	0	—	2	—	1	—
August 5	1927	3	—	5	—	10	—	0	—
	1950	—	0	—	0	—	0	—	0
	2010	—	0	—	0	—	0	—	0
	2033	3	—	4	—	5	—	0	—
August 6	0745	—	1	—	0	—	0	—	0
	0805	9	—	0	—	26	—	0	—
	0830	5	—	0	—	8	—	0	—
	0855	—	2	—	0	—	0	—	0

OS, oil-soaked sponge; WS, water-soaked sponge.

Daylight testing produced differences in flights to the oil-impregnated and control sponges (Table 1). In 105 min of exposure (seven trials) to each of the sponges, the oil-soaked sponge was approached more often than the water-soaked sponge by Wilson's petrels (115:36), Leach's petrels (9:0) and great shearwaters (56:3). Sooty shearwaters (6:12) did not show this preference, but the sample size was small. Five seabirds belonging to other orders, *Morus bassanus*, *Larus marinus*, *L. argentatus*, *Sterna paradisaea* and *Fratrula arctica*, were seen in the area of the tests, but none of them responded to either of the sponges. Insufficient flights prevented analysis for Leach's petrel and sooty shearwater, but Wilson's petrel ($P<0.01$) and great shearwater ($P<0.025$) made significantly more flights to the oil-soaked sponge than to the control sponge (one-tailed Wilcoxon matched-pairs signed-ranks tests⁴).

Their responses to the oil-soaked sponge seem clear evidence that Wilson's petrel, great shearwater, and possibly Leach's petrel and sooty shearwater also, have the ability to follow an attractive airborne odour to its source by olfactory cues alone. The absence of any observed flights to the oil-soaked sponge by other seabird species present during the tests suggests that the petrels and shearwaters alone have this ability.

As shearwaters and petrels are known to be attracted to boat lights during darkness, I worked without lights by using a starlight scope image intensifier to count flights during night trials. Because the image intensifier creates an image by magnifying ambient light intensities electronically it freed results from phototaxis complications. Previous experience with the instrument had shown that although the shearwaters could be reliably identified to species, the petrels could not. Therefore, the latter were treated as one during night testing.

In a test session commencing at 0110, petrels flew upwind to the oil-soaked sponge sixteen times during 30 min (two trials), but no petrel flights to the control were seen during its

30 min of exposure. No shearwater flights were tallied for either sponge.

These results indicate that the petrels (Leach's, Wilson's or both) use olfactory cues in foraging at night as well as in daylight. I saw flying shearwaters through the instrument before and after the test session, making the complete lack of flights to either sponge puzzling. Conceivably, these fast-flying birds could have passed through the limited, stationary field of the image intensifier too rapidly to be seen. In any case, further observation is needed before nocturnal olfactory guidance in shearwaters can be confirmed.

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Operant Study of Sun Altitude and Pigeon Navigation

EVIDENCE that the Sun is involved in pigeon navigation¹⁻⁵ has been interpreted, either partly^{1,7,8} or entirely⁶, in terms of the pigeon's ability to distinguish differences in altitude between the Sun at the home base and at the point of release. Attempts using mirrors to modify the apparent arc of the Sun at the loft⁹ have been inconclusive; although the pigeons showed normal orientation after 10-14 days of this treatment, the birds were old and may have remembered the true path of the Sun. Similarly, experiments in which pigeons have been kept out of sight of the Sun for several days before release¹⁰ have ignored the possibility of memory and, in any case, have produced conflicting results.

In an attempt to clarify the part played by the altitude of the Sun in the discrimination of direction, I have used a technique similar to that of McDonald¹¹, in which a pigeon is confined in a box which can be rotated about a vertical axis. The box was fitted with a key at which the pigeons could peck, and, in field trials at three widely separated sites, rewards were offered when the pigeon was pointing towards the home loft at Bristol, but not when it was pointing in the opposite direction. In other words, birds were conditioned to distinguish the home directions, and the field trials have shown that these birds used Sun altitude as the basis for discrimination.

Fig. 1 shows a pigeon restrained in the conditioning box. A system of pulleys enabled the box to be rotated by remote control about an axis passing through the bird's head; immediately in front of it was a horizontal pecking key, and food reward was offered at a hole beside the key. Contacts between the key and food hopper and the external circuit controlling reward were made through brushes and rings. White noise was funnelled through a tube next to the rotating column. When this conditioning apparatus was used in the field, all landmarks were hidden from the bird's sight by a screen 24 inches in diameter and 8 inches high. This screen was attached to the box and rotated with it, so that it could not provide directional clues.

Tests in the laboratory involved an artificial Sun, provided by a projector lamp placed in a carriage, moving over a track which could be set to produce any required Sun-arc. The conditioning apparatus was arranged so that the bird's head was at the centre of the Sun-path circle, 83 inches from the Sun. A muslin-covered 'Perspex' dome, 3 feet in diameter, was placed over the conditioning apparatus so that (to a human observer) only the "Sun" was to be seen in the artificial sky when the laboratory was blacked out.

The birds used were two homing pigeons which had been trained up to 10 miles from the Bristol University loft. Before the start of the field experiments, they were reduced to 75% of their normal weight and trained to peck the key for food reward on a VR 26 schedule, without sight of artificial or real Sun. Both birds were then trained daily, in sunny conditions, between 1130 and 1330 GMT, at one of three different sites (that is, a different site each day): Ombersley (58 miles north), Oxford (60 miles east-north-east) and Bradnich (60 miles south-west). During each daily session, a bird was given thirty-six trials, each lasting 30 s, in which it was either oriented towards Bristol (and rewarded on a VR schedule for six, sixteen, twenty-six, thirty-six or forty-six responses) or in the opposite direction (no reward) in a randomized sequence. Trials were presented in groups of two to twelve, each group being preceded by 3 min of observation, during which the bird was oriented south with the key covered. Between trials, the bird was slowly rotated, either clockwise or anti-clockwise, through one-half to two complete revolutions.

During 3 weeks only eight sessions were possible because of

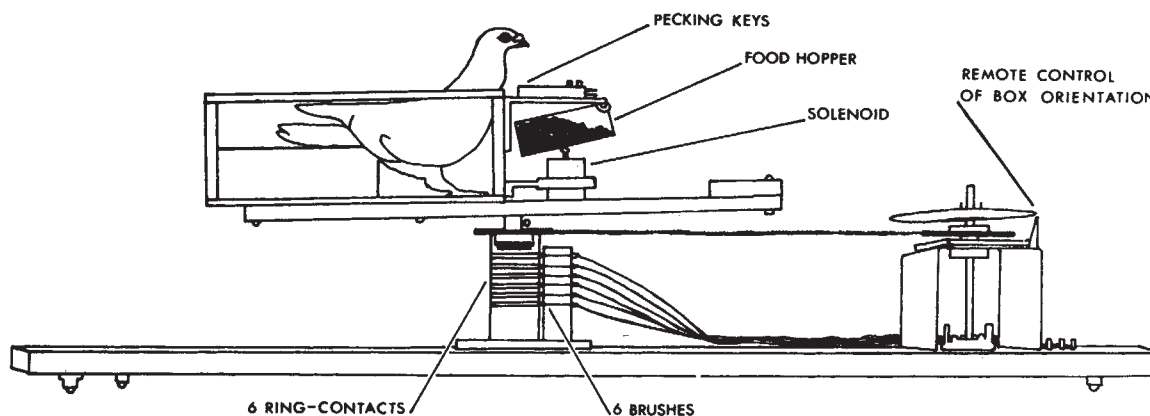


Fig. 1

changeable weather. A sunny spell then permitted continuous training for 6 days, and only four trials were then required to demonstrate discrimination (that is, continued responses to the VR 26 reward situation, but always less than six responses to the no-reward situation).

Did this merely represent extremely quick reversal learning, based on north/south discrimination, or a discrimination between home and non-home, based on comparison of Sun altitude? To answer this question, groups of trials were randomly interspersed with three to four unrewarded trials in which a periscope-type arrangement of mirrors was used to change the altitude of the Sun-arc. This arrangement was set 30 inches from the bird's head, and was surrounded by a screen which made it impossible for the bird to see the true Sun position. It was checked that the mere presence of the periscope had no effect on the distribution of responses. When used at Ombersley, it was set to produce a Sun-arc appropriate for 180 miles south of Bristol; at Bradnich it was set for an arc appropriate for 180 miles north of Bristol. During 7 days, forty-eight tests provided the data in Table 1. Significantly more responses were made in the false home direction than in the true home direction (Mann-Whitney U test).

Table 1 Mean Number of Responses per 30 s made when Faced in False Home Direction (F) or True Home Direction (T)

	Bird G		Bird P	
	F	T	F	T
Ombersley	36.8	11.9	41.5	11.1
	$P=0.053$		$P=0.003$	
Bradnich	42.3	15.8	23.6	12.8
	$P=0.01$		$P=0.015$	
Overall mean	40.1	13.7	30.1	11.8
	$P<0.01$		$P<0.01$	

Both birds were then also tested under the artificial Sun. Sun-arcs appropriate to approximately 300 miles north or south were presented in a random sequence, and responses were rewarded on the VR 26 schedule when the bird was oriented towards the theoretical home. During each presentation session, the bird was oriented south for 3 min with the key covered, then tested for 30 s either towards "home" or in the opposite direction. Ten sessions were presented over a 2 h period during a single day.

In previous experiments, using this schedule (to be described in detail elsewhere), naive birds required several weeks training before discrimination was apparent, but these two birds, after the field experiences described, showed discrimination during this single day's training. After a further four field sessions at Oxford and Bradnich, the birds were tested again, with the same result. Table 2 shows the responses for the latter sessions of both days (sixteen sessions per bird). Unrewarded scores have been compared with the scores required for reward (Mann-Whitney U test).

Table 2 Mean Number of Responses per 30 s made when Faced in Home Direction (H) or Opposite Direction (O)

Bird G		Bird P	
H	O	H	O
26	6.6	26	8.4
$P<0.001$		$P<0.01$	

These pigeons, then, were attending to Sun altitude in making a discrimination between home and non-home directions, in both field and laboratory. The fact that they did so does not necessarily prove that such a discrimination is involved in navigation, but the very existence of such an ability strongly supports such a conclusion.

Tests performed late in the day showed that as the Sun became hidden by the edge of the landmark screen, responses became random, although the position of the Sun could be easily estimated from shadows on the wall of the screen. Thick uniform overcast had the same effect and as a result it was not possible to test for the disorienting effect of magnets demonstrated by Keeton¹² for birds flying freely in overcast conditions. In sunny conditions similar results to those of Keeton were obtained: a bar magnet placed on top of the conditioning box so as to produce a field in the region of the bird's head of 0.5 gauss had no effect at all on the distribution of responses at any of the sites.

A further attempt was then made to demonstrate any ability to orientate under overcast; a third bird was trained under overcast to respond in a simple compass direction (south). Three days of training with seventy-six trials per day failed to produce any sign of discrimination. With the Sun visible, twelve trials were sufficient to show clear discrimination.

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Criteria for the Validation or Invalidation of the Competitive Exclusion Principle

A CONTROVERSY^{1,2} has arisen over the interpretation of the results of an experiment by Ayala³ purporting to invalidate the "competitive exclusion principle" which was defined in terms of the Volterra competition equations. The invalidation was based on a competition experiment between *Drosophila serrata* and *D. pseudoobscura* where the two species were in apparent equilibrium, and from which the following parameters were calculated:

$$\alpha = \frac{K_1 - N_1}{N_2}, \beta = \frac{K_2 - N_2}{N_1}$$

where K is the maximum number of individuals attainable when only one species is present, and N is the number actually observed at equilibrium. These parameters when estimated from Ayala's results were such that stability would not be predicted between the two competing species, and thus the competitive exclusion principle was rejected. Borowsky¹ re-analysed the data, and concluded that a stable equilibrium was not present, and that the depression in yield of the mixed populations was caused by decreased fitness of each species from short term fluctuations in temperature that resulted in an environment optimal for neither species. Ayala subsequently² replied to these criticisms.

We wish, however, to criticize Ayala's conclusions about the nature of the Volterra equations. It seems obvious to us that these equations are an idealized and simplified model of competition between two species. To show that these equations are insufficient to explain, an equilibrium reflects more on the applicability of the equations rather than on the "whole" competitive exclusion principle. The Volterra equations describe competition in terms of first order interactions imposed on idealized logistic growth curves (that is, straightforward competition for a single limiting resource per species) which are rather large assumptions to make for real populations. It is worth noting that other authors^{4,5} have derived different formulations of competition leading to stability between two species.

The Volterra equations show that a necessary (but not sufficient) condition for stability is that the yield of the mixture at equilibrium

$$N_1 + N_2 > \frac{N_1 K_1 + N_2 K_2}{N_1 + N_2} - \frac{N_1 N_2}{N_1 + N_2} \left(\frac{K_1}{K_2} + \frac{K_2}{K_1} - 2 \right)$$

where $N_1 K_1 + N_2 K_2 / N_1 + N_2$ is the expected yield of the mixture calculated from the yield of the species without competition (pure stand yield). When $K_1 = K_2$ stability is not possible if the yield of the mixture is less than that of the pure stands.

When expressed in this way, it is seen that Ayala rejects the competitive exclusion principle since the total yield of the components of the mixed population is far below the yield of the pure stands; but this is insufficient evidence on which to reject the supposition that the two species are limited by different resources or factors. Conversely when the yield of a mixture exceeds the mean yield of the pure stands it is probable that a stable equilibrium will be reached but again there is insufficient evidence for this. In order to analyse competition fully, it is necessary to know the yields of the components of a mixture over a range of input proportions of the components^{4,6-8}. A single proportion is inadequate, as stability will be achieved only if there is frequency dependent selection in the direction of advantage of the minority component, a situation which often results from utilization of different resources.

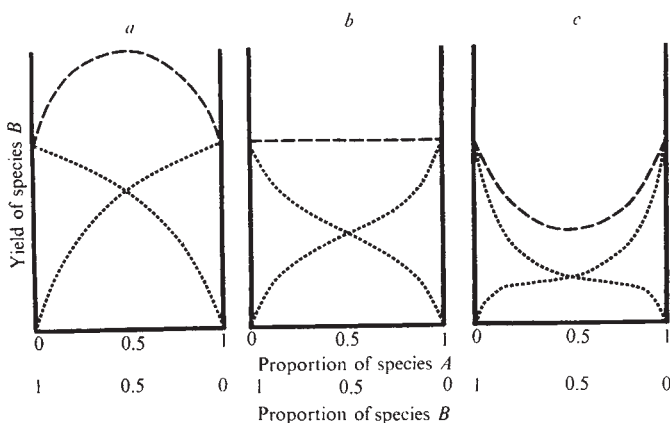


Fig. 1 Replacement series graphs showing the theoretical outcome of competition based on the model of De Wit* (relative crowding coefficients $k_{12}=k_{21}=3$ and equal pure stand yields) with different total yields of the mixtures. The frequency dependent relationship leading to stability between the two species is the same in all cases. ---, Total yield; . . . , yield of components.

It is appropriate to demonstrate this using a counter example, since a fuller discussion of the methodology of competition experiments is in preparation (M. A. Khan, P. D. Putwain and A. D. Bradshaw, unpublished work). Consider three competitive

relationships (Fig. 1): all are frequency dependent in that the minority component is at an advantage; how then can the variations in pure stand yield come about? In Fig. 1a the two components are using different resources, and the mixture can exploit these resources better than either component, and so yield more than the pure stands. Fig. 1b may result from the occurrence of a relationship (like Fig. 1a) between the early stages in the life history of the competitors, but a subsequent limitation of total productivity by a factor common to both species at a later stage. Several possibilities may account for Fig. 1c. For example, there may again be exploitation of different resources in the early stages of the life history, but the mixed populations may be more susceptible to a different environment at a later stage: this may act equally on both species. Another possibility is that there is still niche divergence but that mutual interference in, or lower productivity of, their common niche (for example, production of toxic substances^{9,10}) would lower the total yield (Fig. 2). Although these examples are idealized, sufficient cases are known to indicate that total yields are poor predictors of competitive outcome (refs. 11 and 12 and unpublished work of A. P. C. Seaton) and Ayala^{3,13} himself reports detecting frequency dependent relationships between the two species used in his experiment.

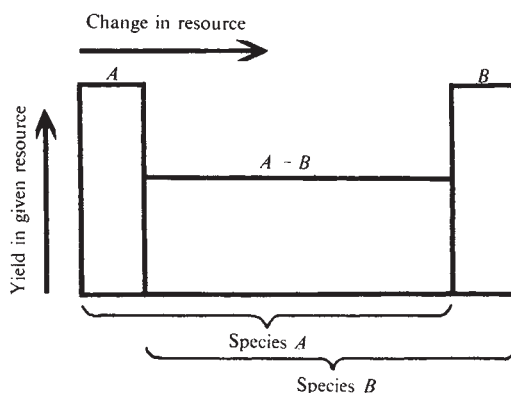


Fig. 2 A naive diagram of a situation which will lead to a stable equilibrium, yet reduced overall yield of a mixture.

Validation or invalidation of the competitive exclusion principle cannot be achieved by showing that a simple theoretical model is not adequately predictive, nor can the stability of species mixtures be deduced without giving the components under a range of frequencies, and measuring the yield of the individual components. We feel in any case that the "competitive exclusion principle" like the "theory of natural selection" is axiomatic¹⁴, perhaps therefore trivial, but not without significance.

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GENERAL

Distillation and Storage of Water

As a consequence of a recent move from one laboratory to another it was necessary to reinstall both primary (metal) and secondary (hard-glass) distillation apparatus. Our first measurements were of the surface potential¹ (V_0) at the air/water interface—a parameter notoriously sensitive to the presence of trace quantities of surface active compounds. The V_0 of the water from our newly-installed stills drifted badly but, from past experience, little time was wasted in tracing the source of the contamination to a short length of polyvinyl chloride (PVC) tubing inadvertently fitted between the primary still and the primary container; a redistillation, in all hard-glass apparatus, failed to eliminate the contaminant. Drift-free, "equilibrium" water (as measured by ultraviolet absorbance, surface tension and conductivity) was immediately restored, when the plastic tubing was replaced by glass. We then obtained samples of "distilled" water from other laboratories. To our consternation but not surprise, many of these samples smelled, frothed, adsorbed strongly in various ultraviolet wavelengths or gave surface tensions as low as 60 dynes/cm. Cursory

examination of their distillation apparatus, or of their reservoir container and/or linkages, revealed an extensive use of plastic of one sort or another. As a warning, Fig. 1 shows the ultraviolet spectra of the material extracted from 1 g of commonly used tubing into 100 ml. equilibrium water at room temperature in 1 h; the inset, for comparison, illustrates the extent of purification of tap-water after a simple two stage distillation in all glass apparatus. Fig. 2 is a tracing of the surface potential (V_0) of equilibrium water and water collected through PVC tubing.

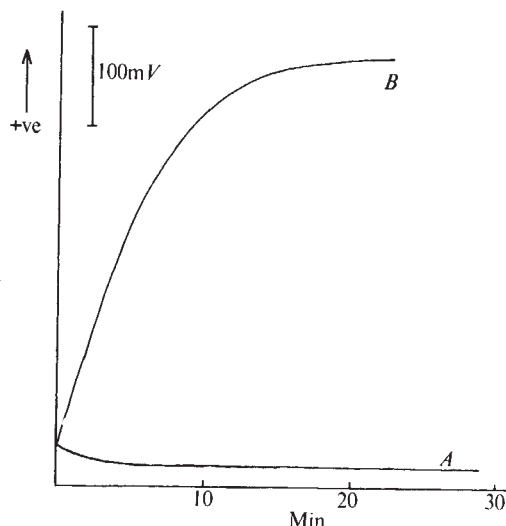


Fig. 2 Continuous recordings of surface potential (air/water) of (A) pure water, (B) polyvinyl chloride contaminated water. The apparatus consists of a small (10 ml. capacity) polytetrafluoroethylene or glass dish shrouded within a small, copper Faraday cage. The surface electrode (High) consisted of an americium foil and the liquid electrode (Ground) was a calomel half cell. Potentials were measured with a Vibron 33 electrometer.

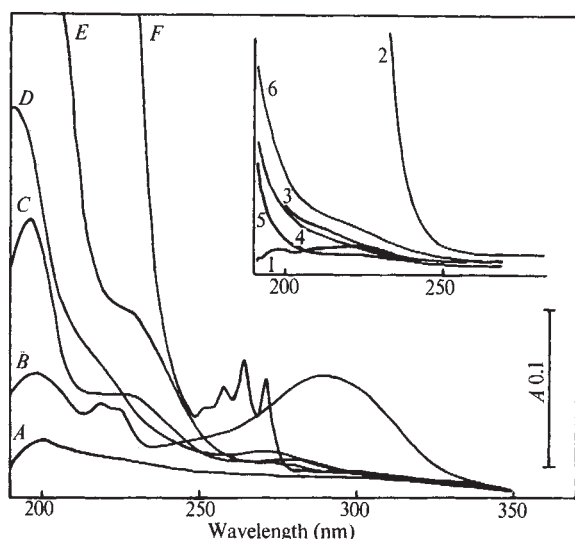


Fig. 1 The ultraviolet spectra of aqueous extracts of various materials compared with equilibrium water. Trace A is the instrument base line with equilibrium water in both sample and reference cuvettes; B, 'Viton' rubber tubing; C, polyvinyl chloride tubing; D, 'Parafilm' closure material; E, silicon tubing; F, nylon tubing. Polytetrafluoroethylene and some samples of polythene produce traces indistinguishable from A. Inset: the ultraviolet spectra of "water" at various stages of purification. 1, Instrument base-line with both cuvettes empty; 2, tap-water; 3, tap-water after one "primary" distillation; 4, primary distilled water redistilled from hard glass; 5, redistilled water distilled again in the presence of KMnO_4 ; 6, 'Analar' water. The reference cuvette contained air.

Granted the old adage that one man's water might be another man's poison, it would nevertheless seem a reasonable philosophy to reduce the exposure of a pure chemical to as few other materials as possible, particularly if they be unknown. The plastic tube and/or container artefact has obtruded into biological research on a number of previous occasions²⁻⁶; our own experience is offered as a salutary example, we hope, to others. If hard-glass were discovered today, all other materials now used in the preparation and storage of water might well be discarded, with the possible exception of polythene and polytetrafluoroethylene, in spite of the very remote possibility of "anomalous water"⁷.

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BOOK REVIEWS

Agricultural Strategy

Two Blades of Grass: Rural Cooperatives in Agricultural Modernization. Edited by Peter Worsley. Pp. xi+395. (Manchester University: Manchester, November 1971.) £4.80.

Agricultural Development: An International Perspective. By Y. Hayami and V. W. Ruttan. Pp. xiv+367. (Johns Hopkins: Baltimore, Maryland, and London, 1971.) \$10; £4.75.

Behavioural Change in Agriculture: Concepts and Strategies for Influencing Transition. Edited by J. P. Leagans and Charles P. Loomis. Pp. xiii+506. (Cornell University: Ithaca and London, November 1971.) \$12.50; £5.95.

THE dominant international issue today is undoubtedly that of the "two worlds", rich and poor, between which the gap is, if anything, widening. The main focus of attention now is on the need to improve the effectiveness of development policies and any additions to the vast and growing body of literature should be judged primarily by the extent to which they contribute to any such improvement. The three books considered here belong to three different streams of thought and are better considered separately rather than comparatively.

Two Blades of Grass is a symposium volume which discusses rural cooperatives and agricultural modernization, dealing mainly with sociological aspects. Two introductory chapters, the second of which poses most of the questions demanding attention, are followed by ten separate regional case studies, four of which have been published elsewhere. Taken individually the papers are instructive, but collectively they do not answer the questions that matter.

In the first place, there is very little reference to the economics and management of cooperatives. In the introduction the editor argues that "It is not the case that increases in scale lead to increased efficiency and productivity"; this comes close to rejecting altogether the economic function of agriculture cooperatives. Where there is an economic comment it is glossed over. Thus Crocombe, discussing the Pacific

Islands, points out that "prestige (and usually financial reward) is much greater for farm owners than for (cooperative) farm managers"—a point worth more thorough examination. Vavislar, writing about India, gives some measures of the economic benefits of a sugar cane factory, but this is not typical of the book. In the event, fundamental economic and managerial weaknesses are the principal factors contributing to the lack of success of cooperative ventures and cannot properly be ignored in a book of this kind.

A second weakness is the lack, even on the non-economic aspects, of any overall analysis and synthesis of the material. There are many thoughts interspersed throughout the book which are capable of general examination. One of the more provocative of these, to be found in the Landsberg and Hewitt paper on Mexico, is that "peasants may be capable of directing their own organizations to a significant degree within as brief (!) a period as twenty to thirty years". The negative inference of this, if true, must be that the global development strategies of UNCTAD for the next decade are over-ambitious.

It may be asking too much of the book to demand a definitive set of conclusions but to quote from one of the introductory chapters: "In the last resort what we want to know is why certain results are expected, given an initial state and a sequence of actions". Major omissions on the economic and analytical aspects, in the last resort, leave the reader groping for answers.

In spite of the general title, *Agricultural Development: An International Perspective* is a book comprising, for the most part, a body of production function analysis with little methodological originality, but presenting some interesting results for the specialist in this field. The book begins with a well-referenced review of development theories, which concludes with the authors' contribution: "We hypothesize that technical change is guided along an efficient path by price signals in the market, provided that prices efficiently reflect changes in the demand and supply of products and factors and that there

exists effective interaction among farmers, public research institutions, and private agricultural supply firms". The snag, of course, is in the provisos. Hayami and Ruttan have in the event defined one important condition for economic development, namely that technical change ought to behave as an endogenous variable.

There follows a set of intercountry comparisons, again well referenced, which lead to the not surprising conclusion that among less developed countries there is plenty of room for productivity increases, while in Japan and USA technological change has behaved itself. There are some case studies on the international transfer of technology, but the logic can become over-assertive. The "Green Revolution" is said to have occurred because "Disequilibria in terms of metaproduction function had accumulated and induced the transfer of scientific research capacity to tropical and sub-tropical Asia"; this seems a rather odd description of that particular story.

In a final section, the book explores some general issues, but most readers will wish to qualify the somewhat simplistic assertions. The book makes too little of the sheer pace of the technological advance in developed countries and the difficulties which this has generated. On the other hand, the problems of less developed countries in practice have been less amenable to simple solutions than was hoped immediately after World War II. Moreover, there will be enormous redeployment problems when the less developed countries achieve dramatic increases in agricultural productivity.

When discussing items like land reform, the authors' conclusion is that "A second error was the stress on equity rather than productivity". . . . In this frame of mind, the authors represent the British agricultural revolution as an "ideal type" of agricultural transformation, but this ignores the suffering of the rural population of the day. One can concede that many institutional reforms in less developed countries have been disappointing, while still acknowledging the claims of equity and

recognizing the political pressures for such changes in newly independent countries.

In brief, then, this book will be useful for teaching purposes. In addition, it will provide some good discussion points for agricultural economists but it is too specialized and lacking in balance for the general reader.

Apart from its length, *Behavioural Change in Agriculture* can be warmly commended to anyone interested in the problems of development. The subtitle "Concepts and Strategies for Influencing Transition" captures the flavour well, for it is a book about theories and ideas bearing on the modernization of traditional agriculture.

This is a symposium volume, constructed with considerable care so that the discontinuities in style and subject matter occur as naturally as in a well conducted debate between eminent specialists. The book comprises eight basic papers supported by responses and summary analyses covering complementarities in macro and micro economic approaches, technology and its utilization, the economy and the polity, social science and development, with a final synthesis of concepts and strategies.

The objective is not to provide blueprint solutions to development problems, but rather to set out an intellectual frame of reference within which decision making can be better undertaken. Sometimes this process takes the form of seemingly irrelevant digression, but before too long the point emerges. Thus reduction of power of the British crown and the evolution of constitutional democracy in Parson's paper on agricultural economics leads to a discussion of the importance of a structure of property rights, where the individual knows within what limits he is free to operate and where the ground rules are not changed dramatically. Contrast this with the situation in many newly independent nations and the point is taken. As the response paper by Morse suggests, however, this is not sufficient. The maintenance of law and order may, in the event, be preserving an institutional framework inhibiting development, so that gradualness may have to give way to revolution. Another issue on which Parsons is consciously one-sided is his advocacy of a structure of family farms or "self-willed entrepreneurs". While it is natural for Atlantic communities to favour this system, to much of the remainder of the world it is alien, and a review of the strengths and weaknesses of any alternatives, such as state control or extended family systems, would have a welcome place in this volume.

Perhaps the least relevant paper is that by Frey on "Development Aspects

of Administration". This explores the nature of power in a fascinating but remote fashion, so that the respondent can write "Frey's brilliant exposition of the concept of power seems to offer few short-run conceptual scaffoldings for the understanding of administrative problems". The complaint may be that an additional paper is required, but in view of administrative deficiencies in many less developed countries, it is a notable gap.

The set of papers on technology and its utilization, together with one of the final papers by Professor Bunting, takes the debate on this subject a considerable way beyond that found in Hayami and Ruttan. Here the reasons why technical change is not endogenous are explored; these include researchers interested only in "pure" science, fragmentation of resources, compartmentalization of disciplines and so on. These difficulties are not, of course, confined to the less developed countries.

With the breadth of coverage in terms of intellectual discipline, the level of the papers and the interaction of ideas, it is difficult to think of any set of readers who will not enjoy and benefit from reading this worthwhile contribution to a subject which will be topical for at least the next decade. S. J. ROGERS

Oil on Waters

Oil on the Sea. Edited by David P. Hoult. Pp. vii+114. (Plenum: New York and London, 1969.) n.p.

POLLUTION of the sea by oil is almost as old as the oil industry itself, but it required a major disaster, the sinking of the Torrey Canyon, to bring it home to us that it could constitute a major problem both to amenity and, more importantly, to marine life. It took a second disaster, the leak from the Santa Barbara off-shore rig, to spell out the need for some good science, new technology and workable legislation.

Since the Torrey Canyon episode there has been a wave of symposia on oil pollution and this book contains the papers from just one of them. Inevitably, the conclusion one draws from reading the papers is that oil pollution is here to stay, at least for as long as oil remains the major source of energy for our industrial society. The papers provide a clear insight into the problem and present some of the methods currently being developed to lessen its effects on amenity and life in the sea. Valuable as such papers are, the real worth of symposia is that they enable scientists, technologists, conservationists, lawyers, economists and even politicians to come together and discuss their problems, exchange views, and

possibly agree that more research is required, while they work out the broad principles on which they can co-operate. Significantly, in this instance, there is little or no mention of prevention; is this perhaps an acknowledgment by the authors of the impossibility of achieving this?

It is fortunate for us, although perhaps not for the oil industry, that oil is clearly visible and therefore easily associated with damage to amenity and at least to some degree as a threat to marine organisms, while other pollutants, equally damaging, can because they are invisible, flow undetected into the sea from sewers and factory effluent pipes. This is not to suggest that oil is unfairly singled out by the anti-pollution lobby, but it does mean that it gets most of their attention.

It cannot be denied that oil is an important pollution source, and with an estimated one million tons finding its way into the sea every year, it must not be under-estimated. Some factions of oil are known to be toxic and even carcinogenic and along with other pollutants are absorbed into the marine food webs and more likely than not are being concentrated somewhere. But where that somewhere is, is currently only a matter for conjecture. Some authorities maintain that oil pollution is one of the most important threats to marine life, while others, with equally convincing arguments, play down the role of oil as a major pollutant. Perhaps the reality lies somewhere between the two.

The oil companies are aware of their responsibilities and are spending millions in trying at least to ameliorate the damage that is or might be caused by their activities. To some environmentalists this looks like whitewashing, but whitewashing or no, the fact of the matter is that the best ideas for tackling the problem have so far come from the oil companies. This is as it should be—after all, they have the best know-how in the field.

However, the Torrey Canyon and Santa Barbara leak demonstrated how unprepared the industrial nations were to tackle major disasters and threats to the environment, and also how a solution to a problem may in itself constitute an even greater problem. The method used to clear the oil from the beaches after the Torrey Canyon mishap caused more damage to marine life than the oil itself. Without the necessary thoroughness in working out solutions, this sort of thing will occur again. While it is true that we cannot wait for the minutiae of science, we should make sure that whatever action we take now does not constitute yet another threat and maybe one of an even greater magnitude.

At the end of the day it seems likely

that oil will continue to constitute a major source of pollution. With some 4,000 tankers now plying the shipping lanes and the prospect of more and larger tankers in the future, oil is bound to get into the sea. The best we can hope for, and this will be achieved only by concerted efforts on the part of industry and government, is to contain the flow and improve the methods of treatment. To this end are directed the efforts of the scientific community, at least those who are taking the trouble to apply their skills to the real problems facing the world of the 1970s, and the publication of their researches will hasten some of the achievements that we can expect to realize.

ARTHUR BOURNE

The Sleepwalker

The Roots of Coincidence. By Arthur Koestler. Postscript by Renee Haynes. Pp. 159. (Hutchinson: London, February 1972.) £2.

APPARENTLY stimulated by Kammerer's ideas of "seriality", Koestler here seeks an "acausal law" to explain the temporal clustering of otherwise unrelated events. Throughout the book Koestler shows a very thorough and very deep misunderstanding of modern physics, of randomness and of the use of statistics. For example, (p. 11) "... theoretical physics has become more 'occult', cheerfully breaking practically every previously sacrosanct 'law of nature' ..."; (p. 80) "Thus when an ESP message in the shape of mindons, psitons or what-have-you impinges on a 'critically poised' neuron, it operates on the quantum indeterminacy level ..."; (p. 57) "On the other hand, the whole conception of matter-waves excludes by definition any medium with physical attributes as a carrier of the waves"; (p. 117) "In each case these are causal factors at work, but they obey laws specific to living substance ..."; (p. 117) "... the so-called second law of thermodynamics—according to which the universe is running down like a clock because all its energy [*sic*] is being steadily dissipated into the random motion of molecules in a gas ...".

Apart from recourse to "scientific" arguments, Koestler falls back on rhetoric to plead his case; for example he lists all the distinguished people who agree with him, apparently unaware of the obvious response, which is to list all those of equal or greater distinction who would not agree. It is hard to review tolerantly and critically a work in which an opinion is worth as much as an experimental result, in which an opinion shared is a fact, and

in which the agreement of two Nobel laureates implies a natural law. Neither does it help to find the omission of salient facts: as evidence for the scientific respectability of parapsychology, Koestler cites the support of Duke University for the Institute of Parapsychology set up by J. B. Rhine; but he does not mention that Duke University has now withdrawn its support. The book is too light and derivative to be worth considering at length, and it is disturbing to find that intelligent people seem to be taken in by such elementary un-reason. The only defence for the layman against such statements as that "ESP is a scientifically proven fact" is in the exposure of the quality of the arguments on which they depend. A reader educated in logical inference and some of the rules of evidence should not be taken in. But I suspect that books like this are successful because they support something in which people want to believe.

ANTHONY ROBERTSON

Natural Number Logic

Mathematical Logic, with Special Reference to the Natural Numbers. By S. W. P. Steen. Pp. xvi+638. (Cambridge University: London, January 1972.) £15; \$45.

THIS book presents an impressively wide survey of many aspects of mathematical logic. Starting with a discussion of formal systems and a careful analysis of the concepts of variable and formula, axioms, rules of procedure and truth, the author proceeds to give accounts of propositional and predicate logic using the Gentzen method of natural inference and Beth's semantic tableau. There follows a systematic progression through a series of formal systems A_{00} , A_0 and A . The first of these is a calculus of equations and inequalities between primitive recursive terms without free variables, and is both complete and decidable. The second system A_0 is constructed from A_{00} by the addition of an existential quantifier; like A_{00} , A_0 is complete, but is undecidable. The third system A contains both a universal and an existential quantifier and is both incomplete and undecidable.

The book contains a detailed study of properties of primitive recursive functions including recursion with parameter substitution, Turing machines and related topics like recursive sets, simple sets and creative sets. There is an account of the Friedberg-Mucnik solution of Post's problem on the existence of two recursively enumerable sets neither of which is recursive in the other, and

of numerous results concerning degrees of undecidability. In an earlier part of the book a formalization of set theory is developed, with a brief account of the axiom of choice (AC), the continuum hypothesis (CH), and the generalized continuum hypothesis (GCH) and reference is made to Godel's proof that (AC), (CH) and (GCH) are all consistent with the axioms of set theory and Cohen's more recent discovery of the unprovability of (AC), and of (CH), within set theory. The final chapter is devoted to model theory, and discusses standard and non-standard models and the use of ultraproducts in constructing models, ending with an outline of Cohen's method of proving the independence of (AC) and (CH) referred to above.

According to the author, the aim is to make exact vague intuitive notions of natural number, preciseness and correctness, and to invent a method whereby these notions can be communicated to others, but these are conflicting objectives and the search for correctness has led the author to introduce a notation which is a barrier to communication; by rejecting the familiar compromise of using a variety of letters as variables and seeking to confine the class of variables to x , x' , x'' and so on, built on the scheme that a variable is x or is formed by accenting a variable, formulae often become intolerably accented, and the less acceptable compromise of writing x'' and x'' for x with four or five accents, as for instance in formula [3] on page 99, results.

A valuable feature of the book is the provision of historical sections which are appended to each chapter and which serve both to give a brief survey of the contents of the chapter and to acknowledge sources, and to point to important new results beyond the scope of the text.

R. L. GOODSTEIN

Palaeodemography

Economy and Settlement in Neolithic and Early Bronze Age Britain and Europe. Edited by D. D. A. Simpson. (Papers delivered at a Conference held at the University of Leicester in 1969.) Pp. 186. (Leicester University: Leicester, December 1971.) £5.

As prehistoric archaeology moves away from the study of artefacts in themselves, and towards the investigation of man's economic and social development, the understanding of early agriculture is everywhere seen as a major objective.

Early Britain has left little direct evidence for farming in the form of plant or animal remains. The picture, therefore, must be reconstructed from secondary evidence: from indications

afforded by settlement pattern suggesting land use, from pedological evidence for forest clearance, from traces of plough marks on old land surfaces preserved beneath burial mounds, and indeed from whatever oblique indications can be recovered.

This collection of the papers presented at a conference in Leicester in 1969 well exemplifies both the problems and the rewards of this approach. Among several valuable papers, P. J. Fowler contributes a useful study of the archaeological evidence for the use of the plough in prehistoric Europe. Don Brothwell writes of diet and bio-social change. Essays by I. F. Smith, I. J. McInnes and D. D. A. Simpson conveniently draw together the very little that we know of settlements and house plans in the neolithic of Britain. And J. G. Evans considers the environment of the early farmers and their impact upon the land. His study brings out the unexpected illuminating information which can be gleaned about both by a minute study of the small land snails preserved in the soil, of which he lists thirty-eight species from a single neolithic site. Not quite "a world in a grain of sand, and heaven in a wild flower" perhaps, but an excellent indication of the really important insights which such meticulous work can bring when more obvious sources of information are lacking.

The whole volume is a good reflexion of the serious thinking that is currently going on in this field, where the interests of palaeodemography and agrarian research now extend back more than four millennia before the Domesday Book.

COLIN RENFREW

Polyreactions

Kinetics and Mechanism of Polyreactions. Edited by F. Tüdös. (IUPAC International Symposium on Macromolecular Chemistry—Plenary and Main Lectures.) Pp. 808. (Akademiai: Budapest, 1971.) £11.

THE IUPAC Symposium on Macromolecular Chemistry for 1969 was held in Budapest. The very large number of short papers were published as preprints; this volume contains the four plenary lectures and the thirty-five main lectures, all now printed in English.

The plenary lectures cover selected but important areas of polymer science. Medvedev concentrated on the comparatively narrow subject of emulsion polymerization. Smets dealt with the synthesis and properties of photo-responsive polymers and also with new types of photochemical polymerizations. Huggins divided his lecture into two parts; the first was concerned with rigid

macromolecules of various types and the second with materials having gradually varying compositions and properties. Goodman and Mark ranged widely; they began with polyamides as fibres and moved to the synthesis of polymers usable at high temperatures, web formation, conformations of proteins and finally the use of polymers as chemical reagents.

The main lectures, all given by persons with high reputations, covered a very wide range of topics; together they form a most useful collection of information and ideas about topics of current importance.

It would have been better if this volume had been available sooner but it must have been difficult to collect all the manuscripts and to prepare them for publication. Professor Tüdös has done well as editor, and his colleague Mrs Boros Gyevi must be congratulated also.

J. C. BEVINGTON

Macromolecules

Macromolecules: Structure and Function. By Finn Wold. Pp. xii+305. (Prentice-Hall: Englewood Cliffs, New Jersey, December 1971.) \$8.75 cloth; \$3.50 paper.

THIS book is part of a series of four under the general title *Foundations of Modern Biochemistry*, the other three books being entitled *Organic Chemistry of Biological Compounds*, *Intermediary Metabolism and its Regulation* and *Physical Biochemistry*. While there are certain advantages in breaking the series up into separate parts there is, as the editors admit, a considerable amount of overlap and the reader of the present book may well be irritated by the rather frequent references to some of the other books.

Finn Wold sets out to explain the progress that has been made towards an understanding of the functional properties of the macromolecules in terms of their completely defined three-dimensional structure. The series of books is meant for students taking a first year course in biochemistry after two years of chemistry and biology, and the philosophy behind them is that they should not be encyclopaedic but should select for the students important principles and illustrate and explain these in some depth. This idea is developed here, where the main concern is with proteins, enzymes, nucleic acids and membranes including the structure of mitochondria.

The presentation is rather unusual for a textbook, for not only are certain aspects of the subject taken in some depth to serve as examples but the author is not afraid to digress and discuss philosophical questions. This is

the kind of approach more usually confined to the lecture, but I found it rather refreshing. I am less certain about the reaction of students, bearing in mind that they will be fresh to the subject. Perhaps in some cases the honesty of the author has led him to leave the readers in a rather confused state and feeling rather let down. This is especially so in chapter 7 on protein synthesis. The students should, however, be encouraged to persevere, for there is much for them to gain.

The book is printed in two colours which is attractive but the arrangement of text and figures could have been better. The price, especially of the paperback edition, is certainly reasonable, but I suspect that one should contemplate the purchase of all four volumes in the series. The original approach of the authors deserves to succeed.

P. N. CAMPBELL

Tropical Medicine

Forty Years of Tropical Medicine Research: a History of the Gorgas Memorial Institute of Tropical and Preventive Medicine, Inc, and the Gorgas Memorial Laboratory. By Willard H. Wright. Pp. xii+426. (W. H. Wright: Washington, 1970.)

THE Gorgas Memorial Institute of Tropical and Preventive Medicine and Gorgas Memorial Laboratory was founded in 1928 by Dr Belisario Porras, three times President of Panama, in memory of General Gorgas of yellow fever fame who died in 1920. The Institute has since been supported by the Governments of Panama and the United States.

Since 1928 much important work has been done on the ecological problems of the tropics. Malaria, arbovirus infections, leishmaniasis and American trypanosomiasis have been the main subjects studied, all from a basic biological point of view. Noteworthy studies are those on leishmaniasis in which the Institute is a world leader. Other triumphs include the demonstration of Aotus (Night) monkeys as important experimental hosts for human malaria which has led to great advances in immunology and chemotherapy.

The book is a series of chapters summarizing annual reports for the past forty years and including a number of biographical reports on leading characters and an appendix of important speeches made over the years.

There is an extensive bibliography of the papers published by the Institute. It is a valuable book both for researchers and medical historians, for many details of research are made available which cannot easily be found elsewhere.

P. E. C. MANSON-BARR

CORRESPONDENCE

Development or Exploitation?

SIR,—Recently (April 28) the weekly magazine *West Africa* published an editorial reviewing Sierra Leone's progress during its first year as a Republic. The editorial suggests that: "Economically the future is much brighter than it was a year ago. The diamond slump is ending; Delco, the iron-ore producer, is expected once more to become profitable; Diminco, the diamond mining company . . . has got off to a good start; large-scale rutile mining is expected to be resumed. The value of the diamond industry to the country is still heavily threatened, however, by illicit diamond digging and by smuggling. In agriculture progress remains slow, but the goal of self-sufficiency inside two years in the staple food, rice, no longer seems unrealistic, and, if Common Market obstacles are overcome, the future for the expanding cocoa and coffee crops is good." It then goes on to say that the value of agricultural exports declined by 26 per cent in the previous year and that the world recession in the diamond market had hit Sierra Leone badly. The article is cautiously hopeful about the future of Sierra Leone's economy.

Like most other countries in tropical Africa, Sierra Leone is dependent on the export of raw materials (minerals and crops) to the rich nations of the world. Economists see the expansion of the EEC as a possible means of countries like Sierra Leone selling more raw materials, and, in the case of mining, this is often described as developing local industries. It is of course no such thing. The truth of the matter is that the more readily available raw materials are being exploited and exported as fast as possible and little thought is being given to the conservation of resources for any future development of manufacturing industries. It seems that we in the developed world are keen to cream off the raw materials in under-developed countries in order to satisfy our own needs as consumers. We seem content to condemn the under-developed countries to the role of producers of raw materials.

It might be (as argued by John Maddox, *Nature*, 236, 331; 1972) that price and demand are likely to shape the future availability of raw materials, but is it reasonable for the profiteers and consumers of the rich countries to persuade or to force the under-developed

countries to sell the best of their resources as quickly as possible? Would it not be more reasonable if a massive effort were made to enable the poor countries to develop real industries rather than to remain as producers of raw materials? If this were done the profits of the already-rich would be reduced and the Common Market might not expand quite so quickly as politicians and businessmen hope, but at least there might be a slight chance of real development in the poor countries.

Yours faithfully

D. F. OWEN

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Educating Scientists

SIR,—The education of scientists is as unscientific today as ever it was. And it is poor consolation that education generally has remained an empirical study, dependent for its success on the devotion or genius of its, usually, unsung heroes.

Your report¹ of A. D. C. Peterson's plans for a "generalist" degree in "Education and Engineering" is yet another evidence of the confused thinking of educationists everywhere. In Australia, first degrees are as unspecialized as any generalist could wish, but in times of recession, or fear thereof, graduates are looking for jobs. Furthermore, the generalist training is far from successful in "teaching students to think". From practical experience, the more rigorous requirements of a specialized honours programme are preferable to the tentative probings of a broad pass degree course, especially in preparation for a "general profession" such as librarianship, where the prime requirement is to acknowledge the ways in which other people think.

Highly technical professions require specialized training, and our social and economic system depends upon an adequate supply of highly qualified graduates in natural science, engineering and so on. However, it is yet to be demonstrated that society itself is as amenable to objective study as the environment in which we exist. Education, general or specialized, does little to develop judgment, intuition, imagination or common humanity. And to develop an appreciation of the com-

plexity of situations, and the possible extent of knowledge, a study dedicated to a narrow field is far superior to a "grab of superficialities."

Universities, and Oxford of all has been the doyen in this respect, can leave the specialist study through the experience of an academic society. Peterson should look again before asking others to leap onto the educational roundabout where theories come and go with cyclical monotony.

Yours faithfully,

G. G. ALLEN

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Western Australia 6102*

¹*Nature*, 236, 321 (1972).

Tenure Decisions

SIR,—I wish to comment on the editorial "Is Tenure Tenable?" (*Nature*, 236, 261; 1972). Abandonment of the tenure system in favour of limited periods of engagement would seem an admirable experiment. I disagree with the editorial, however, regarding the corporate review of re-appointments. In my opinion a corporate review might deal unjustly with those who have made valuable contributions to a university. During periods of extreme economic stress, as we are experiencing in western USA, review procedures can degenerate to the level of public lynchings. To safeguard individuals with limited engagements from arbitrary and capricious corporate action it will be necessary to publish and enforce codes of ethical corporate action in matters of appointment and renewal. Administrators or departments who abuse established review procedures should be considered "Schreibtischtäter" (administrative crooks) and called to account for their actions.

Yours faithfully,

JOSEPH E. CUMMINS

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Lynnwood,
Washington 98036*

Pesticides and Man

SIR,—John Maddox (*Nature*, 236, 436; 1972), in discussing untoward effects of persistent pesticides, states, "There are the strongest possible reasons for pre-

serving as many living species as possible, if only for aesthetic and historical reasons". This excellent statement is followed by one which may, I believe, cause some confusion, namely, "There is however, no reason to think that the damage done to the populations of wild birds by pesticides is as yet comparable to the damage done by hunting, thought to be responsible for the deaths of 2 million game birds a year in North America alone . . ."

To the hunter, and to the game manager, the new environmentalist could and should be a most valuable and numerous ally. How regrettable it is, however, that the sport hunting of game under prudent management schemes now in almost universal application is so often accused of hastening the destruction of species! Let us not forget that North America would never be supporting its abundant game populations were it not for public, and specifically hunter, demand. I can assure your readers that legal recreational cropping does not and cannot endanger the continued existence of any North American game bird. Persistent pesticides, however, are believed responsible for the near complete disappearance of the peregrine falcon from most of its world range, and, as John Maddox points out, for low and possibly decreasing recruitment rates in other species as well.

The "damage" done to cattle populations by butchering is incomparably greater than that done by anthrax. Which, however, demands our greater effort and attention? The definition of the issues is, I believe, the most fundamental problem facing environmental scientists.

Yours faithfully,

A. H. MACPHERSON

Regional Director, Western Region,
Canadian Wildlife Service,
Department of the Environment,
Edmonton

Population

SIR,—While welcoming the recent decline in the birth rate in England and Wales, we are disturbed at the assumption by Mr Wynn in your correspondence columns (*Nature*, 236, 181; 1972) that this is a continuing trend which will automatically lead to long-term stabilization of our population. Demographers do not base their projections on the crude birth rate in any one year, which fluctuates considerably, but on available data on long-term fertility trends, such as the "Family Intentions" Survey¹ mentioned by Aubrey Manning, showing that the "ideal completed family size" desired by women is 2.5 children and that "without economic constraints" this rises to 3.5 children.

We now appear to be experiencing a similar phenomenon to that of the 1930s, when generally adverse economic conditions and widespread unemployment caused parents to postpone their family building. At the time it was feared that a falling birth rate might lead to a decline in population, but the birth rate did not at any time fall to the same level as the death rate. Consequently the long-established trend of natural increase remained uninterrupted², and, as we all know, population has grown considerably since 1931. It would seem that today's "relatively" low birth rate is due not to any desire by parents to have replacement-size families, but to decisions "not to have another child until things get better". Economic factors clearly do affect the birth rate, but who would recommend permanent and widespread unemployment as a desirable method of population control? Neither can it be said that, at this level, it is an effective method—it is worth noting that natural population increase is still running at over 100,000 per year³ and that any increase, however small, cannot be sustained in the long run. With increasing absolute numbers of women entering the child-bearing period, a further decline in the birth rate will be necessary to keep the absolute number of births stable at any given level. It will be interesting to see what happens during the next few years.

Yours faithfully,

ROSAMUND McDOUGALL

Population Stabilization,
18 Bridstow Place,
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¹ Family Intentions, Office of Population Censuses and Surveys (HMSO, 1971).

² Parsons, J., *Population versus Liberty* (Pemberton Books, 1971).

³ Registrar General's Weekly Returns for England and Wales (1972).

PCBs in Copying Paper

SIR,—From the article by Masude, Kagawa and Kuratsune on PCBs in carbonless copying papers (*Nature*, 237, 41; 1972), your readers might receive the impression that PCBs are currently used in carbonless copying papers and, by implication, that users of these types of papers might be exposed to toxic hazards similar to those reported in the mass intoxication incident in Japan in 1968.

In view of the current very understandable concern over the question of environmental toxicants and the viewpoint expressed in *Nature* (236, 433; 1972), we feel that the facts relating to the use of organic solvents in carbonless copying systems should be made known to your readers.

Wiggins Teape are the largest manu-

facturers of carbonless copying paper in Europe, and when PCBs were first reported as persisting in the biomass (*New Scientist*, 32, 612; 1966), the use of these solvents was reconsidered. The Yusho poisoning incident was taken into account, but as this was due to a higher chlorinated PCB with different toxicological characteristics from that used in copying systems, this was not considered to be of direct relevance; considerable toxicological investigation had been undertaken by Wiggins Teape in conjunction with Inveresk Research International on the lower chlorinated PCBs used in copying systems, and it was shown that the use of low chlorinated PCBs as solvents presented no hazard to man in the form and amount used.

Nevertheless, in view of the possible but unascertainable hazard to the environment in the long term, it was decided to seek an alternative solvent for use in carbonless copying systems.

A suitable solvent with similar physical characteristics was chosen and extensive toxicological tests were carried out to establish rapid biodegradation and freedom from toxicity.

Since June 1970, no PCBs have been used by Wiggins Teape in the manufacture of carbonless papers, and we know that other responsible manufacturers of similar papers have followed our lead.

Yours faithfully,

R. E. LISTER

Inveresk Research International,
Inveresk,
Musselburgh,
Midlothian

N. J. M. BENNETT

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Knuckle Walking

SIR,—E. N. Tiratsoo asks (*Nature*, 236, 472; 1972) whether the knuckle-walking situation of football linesmen is different in Chicago. It is indeed, with respect to both "football" and "linesmen". In American football, a line-man is one of the players, often bearing a marked physical resemblance to one of the larger anthropoid apes. At numerous intervals in the course of play he will assume a crouching three-point stance, the forward support being the knuckles of one hand. During these intervals knuckle-walking may occur. This is an unsanctioned activity and may result in a penalty to the offender's side if detected by an official.

Yours faithfully,

JAMES S. PROCTOR

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Obituary

Dr T. H. C. Taylor



DR THOMAS HUGH COLEBROOK TAYLOR, who died on April 14, 1972, was a leading tropical entomologist and a pioneer of the biological control of insects. Starting in 1925 with the control of the coconut moth (*Levuana iridescentis*) in Fiji by the introduction of the Malaysian fly parasite (*Bessa remota*), Taylor subsequently established the eulophid wasp (*Pediobius parvulus*) in the islands to control the coconut leaf-miner, and the coccinellid beetle (*Cryptognatha nodiceps*) to control the coconut scale insect, introductions which effectively controlled these serious pests. He also made early studies in Trinidad of a thrips (*Liothrips urichi*) which he used later in Fiji to control successfully the pasture weed (*Clidemia hirta*). The success derived from the introduction of four such unrelated predator and parasitic insects was largely due to Taylor's skilful field studies and captivity breeding techniques. His book, *The Biological Control of an Insect in Fiji*, made an important contribution to establishing biological control as a possible alternative to the use of insecticides; the method had been pioneered earlier in California and Hawaii and is of considerable interest nowadays with growing public concern over the effect of insecticides on the environment. In a paper for the Jubilee Proceedings of the Association of Applied Biologists in 1935 Taylor expressed the view that biological control seldom works in continental areas and that the method was incompatible with the use of

chemicals. This assessment at the time seemed a correct one, but it met with criticism which has to some extent proved justified owing to techniques developed in the last decades.

T. H. C. Taylor was born in 1901 at Ipswich, and graduated in 1924 with first class honours in zoology in the University of London from what was then University College, Reading. He went straight to Fiji to work on biological control, and in the course of his work travelled widely in Melanesia, Eastern Asia and the West Indies collecting suitable parasites, during which time he became familiar with a wide spectrum of the problems of tropical entomology.

In 1935 Taylor was transferred to Uganda as government entomologist at Kawanda Research Station, where he is still remembered with affection and respect for his work on cotton and coffee pests and their natural enemies. He was awarded a DSc degree in 1937 for work on biological control and in 1944 he returned to England to join the Commonwealth Institute of Entomology and became assistant director in 1946. Here his considerable literary talent was deployed to advantage in the field of scientific publications and his skill as an editor was much in demand.

In 1953, at the invitation of Sir Boris Uvarov, he joined the Anti-Locust Research Centre as deputy director and in 1959 succeeded Uvarov as director. Taylor's tenure of this office was marked by an enlargement of the scope and functions of the centre, already regarded as the main international body for locust research. He travelled widely, especially in Africa, and played a particularly important role in guiding the policies of newly independent countries in the sphere of locust control and research. As technical consultant to the UN Food and Agriculture Organization and to all the major international locust control organizations, Taylor worked hard to promote international cooperation in locust and grasshopper work and his tact, wisdom and knowledge were invaluable in facilitating compromise between the sometimes conflicting demands of science and politics. He was also concerned to promote more overseas work in the Anti-Locust Research Centre and in 1961 when the centre became one of the scientific units of the new Department for Technical Cooperation — now the Overseas Development Administration

of the Foreign and Commonwealth Office—he brought about the formation of a new group of locust scientists especially recruited for work abroad.

He played an active role in the work of several learned societies, notably the Association of Applied Biologists and the Royal Entomological Society of London, serving on the council of the latter from 1949 to 1951. He was also a Fellow of the Institute of Biology.

Taylor's premature retirement in 1962 due to increasing ill-health was a sad blow to the centre and to entomology as a whole, but luckily for the former he remained on the staff as editor, where he zealously guarded the extremely high standards of scientific publication which he had set while director. He also acted as a technical editor for the Food and Agriculture Organization of the United Nations and largely due to his efforts such mammoth reports as that of UNDP/FAO Desert Locust Project, covering eight years of international research on the desert locust, became valuable and readable publications.

Taylor, or "Taggers" as he was known to many generations of entomologists, was in the best and truest senses of the words both a gentleman and a scientist; kindness, courtesy and consideration were part of his nature and these, allied to his foresight and wide knowledge of tropical entomology, enabled him to guide, counsel and assist on problems scientific, organizational and personal, with a skill and tact which were as unobtrusive as they were effective.

Announcements

Miscellaneous

Dr John W. Boag, Institute of Cancer Research, Sutton, has been awarded the L. H. Gray medal by the **International Commission on Radiation Units and Measurements**.

The 1972 A. A. Benedetti-Pichler award has been made to **Professor Lyman C. Craig**, Rockefeller University, for his work in microchemistry.

Beit Memorial junior fellowships for medical research have been awarded to **S. R. Bloom**, **N. J. Brewin**, **D. A. East**, **R. T. Hunt**, **J. B. Wakerley**, **I. H. Maxwell**, and **R. Shields**.

The **Laboratoire de Biochimie du Tissu Conjonctif**, **Equipe de Recherche du**

CNRS, has moved to the Medical Faculty, Université Paris-Val de Marne, 6 rue du Général Sarrail, 94-Cretéil, France.

Dr J. W. Menter, director of research and development, Tube Investments Limited, has been elected treasurer of the Royal Society in succession to Sir Frederick Bawden. Dr Menter has also been appointed a vice-president of the Society. The Right Honourable the Lord Rosenheim has been elected a Fellow of the Royal Society.

International Meetings

June 19-20, **Perspectives in Biomedical Engineering**, Strathclyde (Professor R. M. Kenedi, Bio-Engineering Unit, Wolfson Centre, University of Strathclyde, Glasgow G4 0NW).

June 19-21, **Surface Properties and Surface States of Electronic Materials**, Rolla (Professor William J. James, Graduate Center for Materials Research, University of Missouri-Rolla, Rolla, Missouri 65401, USA).

June 19-23, **Paris Cancer Week**, Paris (Secrétariat de la Semaine Cancérologique, c/o Professeur G. Mathé, Institut de Cancérologie et d'Immunogénétique, Hôpital Paul-Brousse, 14-16 Avenue Paul-Vaillant-Couturier, 94 Villejuif, France).

June 19-30, **Remote Sensing of the Troposphere**, Boulder (Professor S. W. Maley, Electrical Engineering Department, University of Colorado, Boulder, Colorado 80302, USA).

June 21-23, **Disinclinations**, Aussois, Savoie (Dr M. Kléman, Laboratoire de Physique des Solides, Bâtiment 510, Université de Paris, 11 Centre d'Orsay, 91 Orsay, France).

June 21-23, **Experimental Medicine and Surgery in Primates**, Lyon (Dr Jacques

Ruffie, Centre National de la Recherche Scientifique, Centre d'Hématologie, Hôpital Purpan, Toulouse, France).

June 21-24, **Selectivity in Trace Analysis**, Stirling (Society for Analytical Chemistry, 9-10 Savile Row, London W1X 1AF).

June 22-28, **Coordination Chemistry**, Toronto (Professor C. J. L. Lock, Organizing Committee, XIV ICC, Institute for Materials Research, McMaster University, Hamilton, Ontario, Canada).

June 25-30 **Problems in Design and Operation of Motor Vehicles arising from their Impact on Man and his Environment**, London (Congress Organizing Secretary, FISITA 1972, Institution of Mechanical Engineers, 1 Birdcage Walk, London SW1).

June 26-29, **Weather Modification**, Rapid City, South Dakota (Dr Richard A. Schleusener, Institute of Atmospheric Sciences, South Dakota School of Mines and Technology, Rapid City, South Dakota 57701, USA).

June 26-30, **Generation, Compilation, Evaluation and Dissemination of Data for Science and Technology**, Le Creusot (CODATA Conference, c/o Professor B. Vodar, BP 30, 92-Bellevue, France).

Reports and Publications

not included in the Monthly Books Supplement

Great Britain and Ireland

Department of Trade and Industry. Technology and the Environment—Report from Scientific Counsellors, February 1972, No. 2. Pp. 46. (London: Overseas Technical Information Unit, Abell House, John Islip Street, SW1, 1972.) [153]

The Vanishing Lands. Pp. 10. (Southampton: The International Synthetic Rubber Company, Ltd., 1972.) [153]

Factor T followed by Beliefs, Tethered and Untethered and the Pheromones of Fear. By Stefan Themerson. Pp. 59. (London: Gaberbocchus Press, Ltd., 1972.) 80p. [163]

Images from Life. (Publication No. 689.) (London: British Museum (Natural History), 1971.) [163]

The Cleveland Way. By Alan Falconer. (Long-Distance Footpath Guide No. 2.) Pp. 136. (London: HMSO, 1972.) £1.80 net. [173]

Research Associations: The Changing Pattern. Pp. 94. (London: Centre for the Study of Industrial Innovation, 1972.) £1. [173]

Department of Education and Science. Statistics of Education, 1970. Vol. 3: Further Education. Pp. xxvi+100. (London: HMSO, 1972.) £1.90 net. [173]

Other Countries

CERN, European Organization for Nuclear Research. The 300 GeV Programme. Pp. vii+231. (Geneva: CERN, 1972.) [63]

Technical Books and Monographs sponsored by the United States Atomic Energy Commission. Pp. vi+126. (Oak Ridge, Tennessee: US Atomic Energy Commission, Technical Information Centre, P.O. Box 62, 1972.) [63]

US Department of the Interior: Geological Survey. Professional Paper 665: Geology and Mineral Deposits, East Flank of the Elkhorn Mountains, Broadwater County, Montana. By M. R. Klepper, E. T. Ruppel, V. L. Freeman and R. A. Weeks. Pp. iv+66+4 plates. (Washington, DC: Government Printing Office, 1971.) [63]

Australia: Commonwealth Scientific and Industrial Research Organization. Annual Report of the Division of Meteorological Physics, 1970/1971. Pp. 46. (Melbourne: CSIRO, 1972.) [63]

Food and Agriculture Organization of the United Nations. Indo-Pacific Fisheries Council—Proceedings, 14th Session, Bangkok, Thailand, 18-27 November 1970. Section II: Management of Common-Use Resources and the Present Situation in the IPFC Area. Pp. 160. (Bangkok, Thailand: FAO Regional Office for Asia and the Far East, 1971.) [63]

Les Théories Fondamentales en Physique. Fascicule V-12: Subtilités Cruciales en Thermodynamique. Par Jean Rigaud. Pp. 87. (Mexico, DF: Jean Rigaud, Apartado Postal No. 20 049, 1971.) [63]

Geology in the Service of India. By Dr. W. D. West. (Presidential Address, Fifty-ninth Indian Science Congress, 1972.) Pp. 12. (Calcutta: Indian Science Congress Association, 1972.) [73]

US Department of the Interior: Geological Survey. Water-Supply Paper 1903: Surface Water Supply of the United States 1961-65. Part 1: North Atlantic Slope Basins. Vol. 3: Basins from Maryland to York River. Pp. ix+850+1 plate. \$4. Water-Supply Paper 2011: Quality of Surface Waters of the United States, 1967. Parts 1 and 2: North Atlantic Slope Basins and South Atlantic Slope and Eastern Gulf of Mexico Basins. Pp. xvii+982. \$4. Professional Paper 682: Hydrology of Hungry Horse Reservoir, Northwestern Montana. By W. D. Simons and M. I. Korabough. Pp. v+66. 65 cents. Professional Paper 684-A: The Pierre Shale Near Kremmling, Colorado, and Its Correlation to the East and the West. By G. A. Izett, W. A. Cobban and J. R. Gill. Pp. iii+19+1 plate. 70 cents. Professional Paper 688: Sedimentary Features of the Blackhawk Formation (Cretaceous) in the Sunnyside District, Carbon County, Utah. By John O. Maberry. Pp. vi+44+3 plates. 65 cents. (Washington, DC: Government Printing Office, 1970 and 1971.) [73]

The South African Institute for Medical Research. Annual Report for the year 1970. Pp. vii+180. (Johannesburg: The South African Institute for Medical Research, 1972.) [83]

International Commission on Radiation Units and Measurements. ICRU Report No. 20: Radiation Protection Instrumentation and Its Application. Pp. v+60. (Washington, DC: ICRU Publications, P.O. Box 30165, 1971.) \$3.50. [83]

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